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ABSTRACT SECTION

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VIRAL HEPATITIS

MODULATION OF BILE TRANSPORTERS IN TOXIC HEPATITIS.

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Objective. Between 2 to 5% of hospitalized patients have toxic hepatitis (TH). Its pathophysiological mechanisms are unclear and unknown. The roles of various bile transporters [BSEP (pump excretion of bile salts), MDR1 (poly drug resistant protein, which excretes a wide variety of substances across cell membranes) and MRP2, MRP3 (resistance-associated proteins polypill, canalicular expression that play the role of transmembrane substance excretory pump)] in this disease. The aim of this study was to investigate the hepatic production of bile transporters (BSEP, MDR1, MRP2, MRP3) in patients with TH. **Material and methods.** 11 patients with diagnosis of TH were included. The drugs associated with this disease were, tacrolimus, mycophenolic acid, prednisone, allopurinol, paracetamol, ibupruphen, levofloxacin and tradol (Table 1). Data were compared with 11 liver biopsies of patients without TH. The study group included 8 women and 3 men with an age range of 17-73. The detection of bile transporters was made by immunohistochemical technique.

Results. Patients with TH had on biopsy: hepatocellular necrosis, hepatic granulomatous reactions, partial portal inflammation or lobular part, prominent Kupffer cells, intrahepatic cholestasis, steatosis, hepatic eosinophilia and lipofuscin. There is a differential output transport of bile salts, observing a reduction in BSEP and an increased MDR1 and MRP3. No differences were observed in MRP2. **Conclusion.** We observed an increased production of bile salts transporadores in patients with TH. It is unknown what their functional effect on the entity and its potential for therapeutic modification.

POLYMORPHISMS OF IL28B PREDICT THE RESPONSE TO TREATMENT OF CHRONIC HEPATITIS C VIRUS (HCV) INFECTION IN MEXICAN POPULATION

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Introduction. Treatment for HCV genotype 1 with ribavirin (RBV) and pegylated-interferon alpha (peg-IFNα) offers low rates of sustained virologic response (SVR). Some single nucleotide polymorphisms (SNPs) in region for the interleukin 28B (IL28B) gene have been identified as predictors for SRV. Our aim was establish the association between three IL28B SNPs (rs8099917, rs12979860 and rs8103142) and treatment response to peg-IFNα/RBV in a cohort of chronic hepatitis C virus Mexican population. **Material and methods.** A cohort study was performed with 83 chronic HCV patients from Medica Sur Clinic and Foundation in Mexico City, from May 2010 to May 2011. All the patients were treated with peg-INFα and RBV. Data were analyzed by logistic regression, adjusting by age, gender and viral genotype to determine the association of the SNPs with the treatment response. **Results.** The study group included 83 patients with HCV infection. The main genotype was genotype 1 in 70% (n = 58). The overall SVR

Table 1. Modulation of bile transporters in toxic hepatitis.

Case	MDR1	MRP2	MRP3	BSEP	Drugs	Controls	MDR1	MRP2	MRP3	BSEP
1	3+ (P)	3+ (P)	1+ (N)	0 (N)	AC	1	1+ (N)	2+ (P)	0 (N)	1+ (N)
2	1+ (N)	2+ (P)	0 (N)	1+ (N)	PN	2	2+ (P)	2+ (P)	0 (N)	2+ (P)
3	3+ (P)	2+ (P)	0 (N)	0 (N)	TL, PN, G, MP	3	1+ (N)	1+ (N)	0 (N)	1+ (N)
4	3+ (P)	3+ (P)	0 (N)	0 (N)	AC, I, L	4	2+ (P)	3+ (P)	0 (N)	1+ (N)
5	3+ (P)	3+ (P)	2+ (P)	1+ (N)	I, AP	5	1+ (N)	3+ (P)	0 (N)	1+ (N)
6	1+ (N)	1+ (N)	1+ (N)	0 (N)	C, MP	6	1+ (N)	3+ (P)	0 (N)	2+ (P)
7	3+ (P)	2+ (P)	0 (N)	2+ (P)	O	7	2+ (P)	3+ (P)	0 (N)	1+ (N)
8	3+ (P)	2+ (P)	1+ (N)	0 (N)	PN, AC, I	8	3+ (P)	3+ (P)	0 (N)	2+ (P)
9	3+ (P)	2+ (P)	1+ (N)	0 (N)	C, T, G, AC	9	3+ (P)	3+ (P)	0 (N)	2+ (P)
10	3+ (P)	2+ (P)	1+ (N)	1+ (N)	PF	10	3+ (P)	3+ (P)	0 (N)	1+ (N)
11	3+ (P)	2+ (P)	0 (N)	0 (N)	TL, MA, PN, AP	11	3+ (P)	3+ (P)	0 (N)	2+ (P)

Immunohistochemical expression of the bile transporters (MDR1, MRP2, MRP3 and BSEP) and the associated drugs that triggered the toxic hepatitis. Tracolimus (TL), micofenolic acid (MA), prednisone (PN), allopurinol (AP), acetaminophen (AC), pentoxifiline (PF), ibuprofen (I), levofloxacin (L), glibenclamide (G), metoprolol (MP), Clonazepam (C), Ondansetron (O) and tradol(T)]. Positive expression (P), Negative expression (N).

was 32.53% (n = 27). In the group of HVC-1, the SVR was achieved in 27%, and in HVC-2 the SVR was 44%. We found association between the rs12979860 CC with SVR in a codominant model with OR 4.83; 95% CI, 1.12-20.8, P = 0.033. No statistically significant association was reported between SVR and rs8099917 nor rs8103142. In this study, the rs12979860 polymorphism CC, CT and TT was presented at the 24%, 41% and 35% of patients, respectively. **Conclusion.** Mexican HCV-1 infected population treated with peg-INFα and RVB presented low rate of SVR and it was associated with SNP rs12979860 CC. The SVR was not associated with SNPs rs8099917 or rs8103142.

OCCULT HEPATITIS B INFECTION IN HEMODIALYZED CUBAN PATIENTS

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Introduction. The hemodialyzed (HD) patients are at high risk of acquiring an infection by hepatitis B virus (HBV). Occult hepatitis B infection (OBI) is characterized by the presence in serum or plasma of the viral genome (HBV DNA) and antibodies against protein of capsid (anti-HBc) in the absence of the infection marker. OBI harbors potential risk of HBV transmission through hemodialysis. **Purpose.** The aim of this study was to asses OBI in HD patients and to explore possible associations with socio-demographics and clinical variables. **Material and methods.** A total of 709 HD patients from 18 Cuban dialysis units were included in this study. Exposure to HBV (anti-HBc) and HBV infection (HBsAg) were tested in all subjects. The antibody level against HBsAg (anti-HBs) was determined in anti-HBc(+)/HBsAg(-) samples. In sera with anti-HBs < 50 UI/L was quantified HBV DNA and was detected HCV infection and replication. **Results.** The prevalence of HBV infection and exposure were 6.9% and 28.6% in the studied population. Out of 709, 31 patients were anti-HBc(+)/HBsAg(-)/anti-HBs < 50 UI/L. DNA was detected in 18 of 31 patients (58,1%). There was no association with any variable. OBI is frequent in HD patients, especially in those anti-HBc(+)/HBsAg(-) y anti-HBs < 50 UI/L. **Conclusions.** The study suggests that protocol for people under hemodialitic treatment should include anti-HBc and positive ones must be analyzed to detect OBI by molecular techniques. It is the first time this research is done in Cuba and gives useful knowledge for the prevention and control of this illness.

ASSOCIATION BETWEEN TNF AND IL6 POLYMORPHISMS AND RESPONSE TO COMBINATION ANTIVIRAL THERAPY WITH PEGYLATED INTERFERON AND RIBAVIRIN IN PATIENTS WITH CHRONIC HEPATITIS C-PARTIAL RESULTS

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Purpose. To analyze the influence of IL6 and TNF gene polymorphisms in response to antiviral therapy with Pegylated Interferon (Peg-interferon) and Ribavirin (RBV) in patients with chronic hepatitis C. **Material and methods.** We included 68 outclinic patients with chronic hepatitis C. We analized -308TNF (G>A) and -174 IL6 (G> C) gene polymorphisms at promoter region. **Results.** Among 68 studied patients, 20 (29,4%) achieved sustained virological response (SVR) and 48 (70,6%) were non-responders or relapsers (NR/R) to antiviral therapy. In this sample 45 (66.17%) were male and the mean age was 51.4 years. There was a higher proportion of patients with HCV genotype 1, 46 (67.6%), and they were in greater proportion among the NR/R group (p = 0.006). In -308TNF polymorphisms analisis, the G and A allele frequencies were respectively 73% and 27% in SVR group; and these allele frequencies were 90% and 10% in NR/R group, respectively (p = 0.018). The GG, AG and AA genotype frequencies were, respectively, 50%, 45% and 5% among SVR patients; and 81%, 17% and 2% among non-responders/relapsers. The frequencies of predicted phenotypes for high and low producers were 50% and 21% in SVR group; and 19% and 71% in NR/R group (p = 0.016). In -174 IL6, genotype frequencies in SVR group were 45% of GG, 45% GC and 10% CC. In SVR group the genotype frequencies were: 58% GG, 34% GC and 8% CC (p > 0.05). There was not statistical association between IL-6 phenotypical frequencies and response to therapy. **Conclusion.** These partial results suggest that G allele presence in the -308 TNF (G > A) polymorphism is associated with poor antiviral therapy response in patients with chronic hepatitis C treated with pegylated interferon and ribavirin.

INFLUENCE OF POLYMORPHISMS IFN-GAMMA AND IL-10 IN RESPONSE OF PATIENTS WITH CHRONIC HEPATITIS C-PARTIAL RESULTS

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Purpose. To evaluate the possible association between IL-10 and IFN-γ gene polymorphisms and response to combination antiviral therapy with pegylated interferon and ribavirin in patients with chronic hepatitis C. **Material and methods.** This is a case-control study. The 874 IFNG T> A, IL10 (-1082 G> A,-819 C> T,-592 C> A) polymorphisms were genotyped by Real Time-PCR. **Results.** Sixty-eight patients were included and among them 20 achieved sustained virological response (SVR) and 48 were non-responders or relapsers (NR/R) to antiviral therapy; 45 (66.17%) were male and the mean of age was 51.4 years. There was a higher proportion of patients with HCV genotype 1 (67.6%) in this sample and they were in a greater frequency among the NR/R (p = 0.006). In -308IFNG polymorphism analysis, the the T and A allele frequencies were 0.33 and 0.67 in SVR and NR/R groups, respectively (p = 1.00). The T/T (high cytokine producers), T/A (intermediate cytokine producers) and A/A (low cytokine producers) genotype frequencies were respectively 0.10, 0.45 and 0.45 in patients with SVR and 0.15, 0.38 and 0.47 in NR/R group. In analysis of IL10, the possible combinations of polymorphisms at positions -1082, -819 and -592 produce GCC, ACC and ATA haplotypes. To perform statistical analysis, genotypes were grouped according to phenotypes. The analysis showed no significant differences among allele frequencies, phenotypes and response to therapy. Regarding the genotype frequency, the GCC/GCC frequencies observed were 0.15 SVR group and 0.08 in NR/R group. The frequency of ACC / ACC was 0.05 in the SVR group and 0.17 among NR/R patients. The ACC/ATA frequency was 0.40 among sustained responders and 0.17 in NR/R. The frequency of ATA/ATA was 0.14 in the NR/R and there was no patients with this genotype

among sustained responders. There was no statistically significant differences in these analysis. **Conclusion.** This analysis of data showed no association between IL10 and IFNg gene polymorphisms and response to antiviral therapy in individuals with chronic hepatitis C. The small sample size may have influenced these analysis outcome.

EVALUATION OF CLDN1 GENE POLYMORPHISMS IN PATIENTS WITH CHRONIC HEPATITIS C: ASSOCIATION WITH ANTIVIRAL THERAPY RESPONSE-PARTIAL RESULTS

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Purpose. Claudin-1 (CLDN1) is part of the family of integral membrane proteins involved in occlusion junctions structure and their variations. They are found in gene regulatory regions and might have a role in HCV infection changing the susceptibility to virus and, consequently, the viral clearance. The aim of this study was to evaluate the possible association between CLDN1 gene polymorphisms in patients with chronic hepatitis C and response to combination antiviral therapy with pegylated interferon and ribavirin. **Material and methods.** This is a case control study. Two single nucleotide polymorphisms of the gene CLDN1 [rs98482283 (IVS-2983) and rs9865082 (-7153)] were studied. **Results.** In rs98482283 (IVS-2983), the allele C frequency was 29.7% in nonresponders/relapsers group (NR/R), while the frequency among virologic sustained responders was 18.8%. Individuals with C allele had 1.83 more chance to be in NR/R group, however there were no statistical significant in this analysis (p = 0.12, OR = 1.83). At rs9865082 (-7153), G allele was found in 85.4% in NR/R group, while in NR/R group G allele frequency was 93.3%. The A allele frequency was 14.6% in NR/R group and 6.7% among sustained responders patients. Despite the higher G allele frequency suggests some protection (OR 0.42), there was no statistically significant association (p = 0.35). **Conclusion.** The CDLN1 polymorphisms in rs98482283 (IVS-2983) and rs9865082 (-7153) were not statistically associated with response to therapy, but the partial results suggest the CDLN1 could be a potential prognostic marker to therapy response in individuals with chronic hepatitis C.

ASSOCIATION BETWEEN IL28B GENE POLYMORPHISMS AND ANTIVIRAL THERAPY RESPONSE IN PATIENTS WITH CHRONIC HEPATITIS C: PARTIAL RESULTS

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Purpose. The IL28B gene polymorphisms have been studied in patients with chronic hepatitis C in an attempt to find better prognostic markers that influence clinical outcome, particularly, response to treatment. This study evaluated the association between the IL28B polymorphism (rs12979860) and combination antiviral therapy with pegylated interferon and ribavirin in patients with chronic hepatitis C. The secondary aim was to evaluate if the IL28B polymorphisms can be a marker of liver fibrosis (liver biopsy were analyzed according to Metavir score: F0-F2 = mild liver fibrosis; F3-F4 = advanced liver fibrosis). **Materials and methods.** It is a case-control study. 166 patients with chronic infection with HCV genotype 1 were included, older than 18 years, with liver biopsy (analyzed by METAVIR score). They were treated with antiviral therapy with pegylated interferon/ribavirin previously. **Results.** 60 patients had sustained virological response (SRV) to antiviral therapy and 106 were nonresponders/relapser (NR/R). In the IL28B analysis, patients with CC genotype had higher rates of SVR (64.1%) while those with CT and TT genotypes had 26.9% and 29.4%, respectively (p = 0,000172). In this sample, 143 patients were included in liver fibrosis analysis; 72 had METAVIR < F2 and 71 of them F3/F4. According to IL28B genotypes, 42.4% of CC patients had Metavir score < F2 and 57,6% of them were F3/F4; 51.9% of patients with CT genotype had Meravir < F2 and 48.1% had F3/F4; among patients with TT, 54.8% had Metavir < F2 and 45,2% had Metavir score F3/F4 (p = 0.561). **Conclusion.** In the present study, in agreement with international data, the CC genotype of IL28B gene (rs12979860) was associated with sustained response to combined treatment with peg-interferon and ribavirin. The IL28B gene polymorphisms (rs12979860) were not associated with liver fibrosis in these patients with chronic hepatitis C.

IMPACT OF SUSTAINED VIROLOGIC RESPONSE ON QUALITY OF LIFE IN CHRONIC HEPATITIS C VIRUS CARRIERS: SYSTEMATIC REVIEW AND META-ANALYSIS

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Purpose. We sought to create a meta-analysis and to review systematically the evidence in literature of health-related quality of life (HRQOL) changes caused by sustained virologic response (SVR) in chronic hepatitis C virus carriers. **Material and methods.** A PubMed search was performed using the keywords "Hepatitis C", "Quality of Life" and "Therapy". The reviewers came to a consensus on articles that were selected to full reading and should be included in the study. A meta-analysis was performed of mean change difference between responders and non-responders. The Q test was used to assess statistical heterogeneity and the I2 statistic for measuring the degree of inconsistency. Egger's test was used to evaluate the possibility of the occurrence of publication bias. **Results.** Eleven studies were included in systematic review and four in meta-analysis. Nine studies showed more favorable outcome for responders. The meta-analysis showed that the general health and vitality domains had statistically significant mean change difference between responders and non-responders. **Conclusion.** There is evidence indicating that SVR is accompanied by an improvement in HRQOL and patients reaching SVR have clinically relevant improvement in domains of general health and vitality. Moreover, in most studies which patients were unaware of response to treatment, patients with SVR have a better outcome than non-responders, indicating that knowledge of SVR alone does not explain the difference in HRQOL between these two groups.

HIGH PREVALENCE OF OVERWEIGHT IN PATIENTS WITH CHRONIC VIRAL HEPATITIS B OR C

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Background. The prevalence of nutritional disorders in patients with chronic viral hepatitis ranges from 20% (obesity) 1 to 80% (malnutrition) 2. Obesity can accelerate the liver viral damage. Hence, the aim of this study was to evaluate the nutritional status of patients with chronic hepatitis B or C. **Material and methods.** 178 patients with confirmed viral hepatitis C (anti-HCV and HCV RNA positive) (n = 126) or B (HBsAg positive) (n = 52) were prospectively included. The nutritional assessment consisted of body mass index (BMI-kg/m^2), measurement of triceps skinfold thickness (TSF), waist circumference (WC) and percentage body fat (% BF). This study was approved by the Ethics Committee of UFMG. Data were analyzed by SPSS 16.0. **Results.** 82/178 (46.1%) were men and 96/178 (53.9%) women, mean age 50.7 ± 11.5 years, 25 (14%) with compensated cirrhosis. By BMI and TSF patients were classified as underweight (10/178 [5.6%] and 64/176 [36.4%]), overweight (84/178 [47, 2%] and (72/176 [40.9%]) and eutrophic (84/178 [47.2%] and (40/176 [22.7%]), respectively. By WC, the cardiovascular risk of 122 patients was low in 64 (52.5%) high in 23 (18.9%) and very high in 35 (28.7%). The percentage of BF evaluated in 85 patients was below average in 18 (21, 2%), above average in 22 (25.9%) and high level for obesity-related diseases in 45 (52.9%). No significant differences in nutritional assessment of patients with HBV or HCV ($p > 0.20$) were noted. In both groups, significant association was observed among cardiovascular risk and overweight by BMI (OR, 23.1, 95% CI, 9.0-59.1, $p < 0.0001$), TSF (OR, 4.9, 95% CI, 2.3-10.7, $p < 0.0001$), and risk of diseases associated with obesity by BMI (OR, 14.6, 95% CI, 4.9-42.3, $p < 0.0001$) and TSF (OR, 4.9, 95% CI, 2.0-12.4, $p < 0.0001$). **Conclusion.** The high prevalence of overweight and its potential complications in patients with chronic hepatitis B or C reinforce the importance of the nutritional assessment aiming the early diagnosis and specific treatment of these disorders in clinical practice.

NUTRITIONAL DISORDERS IN PATIENTS WITH CHRONIC VIRAL HEPATITIS B OR C

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Background. The nutritional disorders, especially obesity and malnutrition are common in patients with chronic viral hepatitis B and C. However, the prevalence and clinical significance are not well established. Hence, this study aimed to investigate the nutritional status and its association with severity of liver disease. **Material and methods.** 192 patients with chronic hepatitis B (n = 56) or C (n = 136) were prospectively included in their pre-treatment evaluation. Nutritional status was determined by subjective global assessment (SGA), body mass index (BMI) and body fat percentage (BF%). The liver biopsies were scored by METAVIR and cirrhosis, if present, was classified by Child-Pugh. The study was approved by the Ethical Board of UFMG. **Results.** 89/192 (46.4%) were men, 103/192 (53.6%) women, mean age 50.8 ± 11.4 years. 33 (17.2%) patients were diagnosed as cirrhotic by clinical and/or histology criteria (72.7%, 18.2% and 9.1% Child-Pugh A, B and C, respectively, ascitis in 7.3%). The METAVIR scores of liver biopsies (n = 61) were: A0-1: n = 32 (52.5%), A2-3: n = 29 (47.5%), F0-2: n = 46 (75.4%) and F3-4: n = 15 (24.6%). By BMI, 12/192 (6.3%) were classified as underweight, 90/192 (46.9%) as overweight or obese, and 90/192 (46.9%) as eutrophic. The BF% was below average in 21/96 (21.9%), above average in 24/96 (25.0%) and risk for obesity-related diseases in 49/96 (51.0%). Nutritional status, assessed by the SGA, revealed that 12/ 33 patients (36.4%) had malnutrition associated with cirrhosis (OR 3.6, 95% CI, 1.5-8.2, $p = 0.002$), 8 (24.2%), being 3 (9.1%) classified as Child-Pugh C ($p = 0,05$). 12/96 (12.5%) malnourished patients had low % BF (OR, 7.0, 95% CI, 2.4-20.2, $p < 0.0001$). **Conclusion.** Despite the known association of malnutrition with more advanced liver disease, about 50% of patients with hepatitis B or C have overweight, obesity and high body fat percentage. This study reiterates the importance of nutritional assessment in clinical practice for early detection and management of nutritional disorders in patients with chronic hepatitis B or C given its negative impact on the outcome of liver disease.

PREVALENCE OF MAJOR DEPRESSIVE DISORDERS IN PATIENTS WITH CHRONIC HEPATITIS C AND PSYCHOMETRIC PROPERTIES OF HADS AND HDRS SCALES FOR THE SCREENING OF DEPRESSIVE DISORDERS

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Purpose. To estimate the prevalence and associated factors of major depressive disorder (MDD) in patients with chronic hepatitis C. To evaluate the psychometric characteristics of the Hamilton depression scales (HDRS) and the Hospital Anxiety and Depression Scale (HADS) for the diagnosis of depression in this population. **Material and methods.** 120 patients with chronic hepatitis C (52 male and 68 female) were included. They underwent psychiatric investigation through a clinical structured interview MINI-Plus. Clinical, laboratory and socio-demographic factors were compared between groups. The psychometric properties of HADS and HDRS scales were assessed for use in this population. **Results.** The mean age was 53 ± 11 years. The average time of diagnosis of infection was 23 ± 10 years. 22 (16.4%) patients had liver cirrhosis. The most frequent psychiatric disorder was MDD (n = 41, 30.6%). In multivariate analysis, factors that correlated with MDD were: previous episode of MDD (PR = 2), anxiety disorders (PR = 2.5) and diabetes (PR = 1.9). The HADS showed good agreement (Kappa = 0.639) and area under the ROC curve of 0.903; low sensitivity (67.6%) and high specificity (93.2%) using a cutoff of eight. The HDRS showed good agreement (Kappa = 0.664) and area under the ROC curve excellent (0.931). The sensitivity and specificity were respectively (91.9% and 80.0%). **Conclusions.** MDD is the most frequent psychiatric comorbidity in patients with hepatitis C and is significantly associated with anxiety disorders, diabetes and previous history of MDD. HDRS and HADS showed good agreement with the clinical diagnosis of MDD.

THE IMMUNOLOGICAL PROFILE OF COINFECTION WITH HUMAN T LYMPHOTROPIC VIRUS TYPE 1 AND HEPATITIS C VIRUS

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Purpose. Coinfection by hepatitis C virus (HCV) and human T-lymphotropic virus type 1 (HTLV-1) has been reported in

multiple geographical regions and is a result of the similarity in the transmission pathway of both viruses. The objective is to assess and describe the clinical, epidemiological and immunohistopathological aspects of this coinfection. **Material and methods.** Cross-sectional study from 44 patients –23 coinfected by HCV and HTLV-1 (group 1), 21 monoinfected by HCV (group 2) and 20 monoinfected by HTLV-1 (group 3)– submitted to a clinical-epidemiological and laboratorial survey (cytokine profiles and autoantibodies). **Results.** There were no clinical or anthropometric differences between the groups. There was a higher serum concentration of IFN gamma in serum samples from the group 1 as well as a higher degree of hepatic steatosis when compared with the group 2 ($p < 0.01$), but the group 3 presented greater levels of IFN gamma. There was also a higher concentration of total protein and globulin in the group 1 ($p < 0.01$). The production of IL-2 on the group 1 presented an average of 6.37 pg/mL, *vs.* 8.71 pg/mL on group 3 ($p < 0.05$). There was a higher prevalence of mild or moderate stages of liver disease among the group 1 and a larger number of patients with cirrhosis in group 2. **Conclusions.** The TH1 response induced by infection by HTLV-1 proved to be less intense when associated to the infection by VHC, suggesting that coinfection may result in a different pattern of HCV infection due to the immunological disorders associated with HTLV-1.

POSTTRAUMATIC STRESS DISORDER AND QUALITY OF LIFE IN HEPATITIS C PATIENTS

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Purpose. To investigate the impact of posttraumatic stress disorder (PTSD) symptoms on health-related quality of life in hepatitis C virus-infected subjects. **Material and methods.** The sample of the study was 79 consecutive hepatitis C-infected outpatients. The diagnosis of mental disorders was obtained using the Mini International Neuropsychiatric Interview, Brazilian Version 5.0.0 (MINI PLUS), PTSD was diagnosed from the scores of the Brazilian version of the PCL-C and Trauma History Questionnaire (THQ); the Short-Form 36 (SF-36) was used to measure the quality of life. **Results.** Roughly 14% of patients showed PTSD symptoms. The results demonstrate a significant association between the presence of PTSD and quality of life, notably, patients with partial PTSD have impairments intermediate between the absence of full PTSD and PTSD ($p = 0.02$). The bivariate analysis showed a negative impact of PTSD symptoms in the following SF-36 domains: bodily pain, general health, vitality, social aspects, emotional aspects and mental health. **Conclusion.** This study demonstrated that PTSD is a disorder that causes significant impairment in quality of life of patients with chronic hepatitis C, even after controlling for confounders. These results reinforce the importance of vigorously investigate aspects of mental health of these populations as the presence of traumatic experiences and posttraumatic stress disorder.

TREATMENT OF CHRONIC HEPATITIS DELTA WITH PEGYLATED INTERFERON-ALPHA PLUS ENTECAVIR IN PATIENTS FROM WESTERN AMAZON REGION, BRAZIL. WEEK 24 INTERIM ANALYSIS

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Background and aims. The HDV is a defective RNA virus. In other Amazonian countries, was described HDV genotypes I and III. Hepatitis D is the only form of viral hepatitis for which there is not an established treatment, however several therapeutic strategies can be employed. The current study aims to report preliminary results for clinical trial using pegylated interferon-alpha plus Entecavir in patients followed. **Material and methods.** Patients with chronic HDV, defined as anti-HD IgG positive and HDV-RNA positive, were prospectively included for treatment with 180 μg PEG-IFN-α 2a plus Entecavir 0.5 mg day for 48 weeks and followed for 24 weeks. Investigations included baseline level serum HBV-DNA and HDV-RNA and kinetic for 4, 12, 24 and 48 week, determination of HBV and HDV genotypes and histological evaluation. HBV-DNA and HDV-RNA level was assessed by RT-PCR. This is week-24 interim analysis. **Results.** Tirty seven patients were screened and enrolled. 28% white, 5% black, and 67% Amerindians; 56% female; mean age 45.3 years; 61% HBV-DNA positive with mean baseline 5.674 UI/mL and HDV-RNA baseline was 135,768 copies/mL. HDV genotype III was detected in all patients. Fibrosis score none to mild A1 20% F1 36%; moderate A2 68% F2 40% F3 12%; severe A3 12% F4 12%. All patients were positive HBV-DNA in 4-week including negative baseline patients. Twenty seven patients completed 24-week of treatment and twenty seven was HDV-RNA negative. **Conclusion.** Combined treatment with PEG-IFN-α 2a plus Entecavir, resulted in high early virologic response rates in co-infected HBV/HDV patients with genotype III.

INTERFERON LAMBDA SERUM LEVELS IN PATIENTS WITH CHRONIC HEPATITIS C VIRUS INFECTION AND ITS RELATIONSHIP WITH THE RESPONSE TO ANTIVIRAL TREATMENT AND IL28B POLYMORPHISMS

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Purpose. To measure serum levels of interferon lambdas (IL28A/B and IL29) in chronically infected hepatitis C virus (HCV) patients under peginterferon plus ribavirin therapy. **Material and methods.** We studied 45 infected with genotype 1 HCV patients, quantifying levels of IL28A/B and IL29 by ELISA before and at 12 weeks of treatment, and comparing between patients who developed a sustained virologic response (SVR) and non-responders (NR). Furthermore, it was evaluated the IL28B polymorphisms (rs12979860 and rs8099917). **Results.** Groups were comparable in age, male/female ratio and baseline viral load. IL28A/B and IL29 measurement was not significantly different between patients with SVR and NR in samples at baseline and at 12 weeks of treatment. The rs12979860 CC allele carriers had a tendency to higher IL28A/B ($p = 0.171$) and IL29 ($p = 0.068$) levels than non-CC carriers in baseline samples, and IL29 at 12 weeks ($p = 0.086$). Regarding SNP rs8099917, the TT allele had a higher levels than non-TT of IL28A/B (93.6 pg/mL + 44.4 *vs.* 15.2 pg/mL + 4.7; $p = 0.005$) and IL29 (853.1 pg/mL + 754.8 *vs.* 47.2 pg/mL + 15.2; $p = 0.05$) levels, in baseline samples. In samples at 12 weeks, IL29 levels had only a tendency to higher levels in TT carriers than in non-TT ($p = 0.057$). **Conclusion.** We did not obtain differences in levels of IL28A/B and IL29 associated at the response to treatment, so its use as a prognosis and treatment monitoring tool seems limited. The higher levels in good

responder alleles could are more related to an infection protective mechanism, but not involved in the antiviral therapy.

HIGH PREVALENCE OF CHRONIC HEPATITIS B HBEAG NEGATIVE IN BELO HORIZONTE, BRAZIL

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Objectives. This study evaluated the virological and clinical characteristics of patients with chronic hepatitis B (CHB) and in Belo Horizonte, Brazil. **Material and methods.** Demographic and clinical data of 235 patients with CHB in replicative phase (HBVDNA > 2,000 IU/mL) were analyzed in a cross-sectional study. **Results.** 156 (66.4%) patients were HBeAg negative. Comparative analysis between HBeAg negative and positive patients were, respectively: 66% and 84.8% males ($p = 0.002$), mean age 44.7 ± 11.2 and 42.8 ± 14.6 years ($p = 0.16$), median ALT levels 71 *vs.* 117 IU/mL ($p < 0.001$) and median HBVDNA levels 3.3 x 107 IU/mL *vs.* 6.5 x 108 IU/mL, ($p < 0.001$). Lower prevalence of cirrhosis was observed in HBeAg negative patients (38.5% *vs.* 58.2%, $p = 0.004$), but no differences were found in patients with HCC (6.4% *vs.* 10.1%, $p = 0.31$). Age > 40 years (PR = 2.91, 95% CI = 1.87 to 4.54, $p < 0.001$), male gender (PR = 2.00, 95% CI = 1.30 to 3.09, $p = 0.002$) and alcoholism (PR = 2.03, 95% CI 1.56 to 2.64, $p < 0.001$) were risk factors for cirrhosis regardless the status of HBeAg. By univariate analysis, cirrhosis ($p = 0.003$), older age ($p = 0.043$) and alcoholism ($p = 0.025$) were risk factors to HCC, but only cirrhosis was the risk identified in multivariate analysis (PR = 16.29, 95% CI 2.60 to 102.19, $p = 0.003$). **Conclusions.** The prevalence of HBeAg negative CHB in Belo Horizonte is higher than HBeAg positive. HBeAg negative had lower levels of HBVDNA and ALT. Cirrhosis had higher prevalence in male individuals above 40 years and was the risk factor for HCC regardless of the status of HBeAg.

CURRENT STATE OF A SELECT POPULATION OF PATIENTS INFECTED BY HEPATITIS C VIRUS. CUBAN EXPERIENCE

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Purpose. The incidence reported in Cuba by hepatitis C virus (HCV) is considered low, the purposes of the study were identifying the epidemiological characteristics of a select population of patients infected by HCV. **Material and methods.** The research was designed as a cross sectional study of 207 patients with positive RNA detected by PCR techniques and conducted at the National Institute of Gastroenterology during the last two years, 2009-2011. The epidemiological, clinical, virological characteristics and more common histopathological diagnoses were recorded. SPSS statistical software was used to carry out statistical analysis. **Results.** The infection was present in 110 womans/ 97 males, the average age was 48 ± 9.6 years, a greater part of them was original from the western regions of the country. The surgical, odontological treatments and blood transfusions were the most frequent probable transmission patterns infection identified in 79.7%, 68.6% and 46.4%. The time of evolution of HCV infection since first clinical or laboratory findings to the detection of the virus was dated around 4.26 years, only 25.6% have had a past history of anti-hepatitis B immunization. 74.4% have not had any kind of treatment before with antiviral drugs. The most frequent symptoms were asthenia, arthralgia, and elevated transaminases. Genotype 1b is the most prevalent one in the sample, identified in 92.5. The histopathological diagnoses evidenced 90% with chronic hepatitis and 7.7% with liver cirrhosis. **Conclusions.** Because the social and ethics implication of HCV infection, it's important to apply the epidemiological control programmes in the current clinical practice.

EFFECT OF THE TREATMENT OF HEPATITIS C WITH INTERFERON (IFN) AND RIBAVIRIN (RBV) IN THE BODY COMPOSITION MEASUREMENT BY DEXA IN HIV-HCV COINFECTED PATIENTS

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Background. HIV infection and the antiretroviral therapy (ART) have been associated with lipodystrophy (LD), and IFN has been shown to be associated with weight loss, sometimes of difficult recovery once completed. We unknown the effect of this treatment on the body composition, mainly body fat, in a group of patients, as HIV-infected, already with a degree of LD. **Purpose.** To assess the body composition in HIV-HCV patients that start treatment with IFN/RBV and the changes at its ending. **Material and methods.** Pilot and prospective study of HIV-HCV patients. We performed (baseline and at the end of treatment) clinical and laboratory parameters, HIV and HCV-related, as well as HCV-PCR 24 weeks after the completion of treatment to assess SVR. Total and regional body fat contents were measured in the same periods with DXA (Dual energy X-ray absorptiometry) scanners. For LD diagnostic we used the definition of fat/mass ratio (FMR): absence, when is < 1, obvious when is > 1.5, and between 1-1.5 it could have LD but is better to see the evolution. Data are expressed in median. **Results.** We have included 10 male patients; age 45 yo; time on ART 115 months. HIV VL < 20 in 9; CD4 count 577/mm^3. Genotype 1 in 8, and 3 in 2. Time on IFN/RBV: 10 months. SVR in 6 patients. At the end of the treatment we observed a decrease in the level of total, HDL and LDL-cholesterol (expressed in percentage: 4, 16 and 1.5 respectively) and a slightly increase in the level of TGR (9%). The total body mass decreased 7% (from 76.2 kg to 70.6), the total body fat decreased 18.4% (from 21.060 g to 17.172) and the total lean mass decreased only 3%. When the results are expressed in percentage and by regional parts we observed also a decrease in all the parameters: 11% in total body fat (from 26.3 to 23.4), 6% in the fat in arms (21.9 to 20.5), 10% in total fat in legs (22.5 to 20.3) and 12.5% in total trunk fat (30.3 to 26.5). The FMR also decreased from 1.5 to 1.4. **Conclusions.** In these patients, due to ART, we observed a trend to LD at baseline, as the FMR was 1.5. After 10 months on treatment with IFN/RBV there was a decrease in the total body mass (7%), mainly due to the loss of total body fat and less in the lean mass. Regarding the percentage of fat loss, we observed the biggest decrease in the trunk fat and the lesser in the limbs fat. So, the FMR also decreased. This effect doesn't get worse the baseline LD, on the contrary it improves it, although very slightly (decrease of 0.1 in FMR), and could serve to advise the patients and not to be afraid of a possible worsening of LD. The study is ongoing and the next objective will be to perform DXA one year after the end of treatment and to expand the cohort to study clinical or laboratory factors related with these results.

TREATMENT OF HEPATITIS C AND DIRECT ANTIVIRAL AGENTS IN A CLINICAL SETTING

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Aim. To observe the response to therapy with Interferon, ribavirin and protease inhibitor (DAA) in the clinic as compared to results reported in clinical trials. **Material and methods.** 48 consecutive patients with chronic HCV, genotype 1 were treated with triple therapy (36 with Telaprevir, 12 with Boceprevir) following FDA guidelines. Patients were monitored to observe on-treatment and sustained viral response, as well as side effects. **Results.** Of the 48 patients, 60% were men, 15 (31%) were treatment-naive, 24 were previous non-responders and 9 relapsers. The mean age was 54.5 years (69% were older tan 50). The IL28B was CC in 12%, CT in 67% and TT in 21%. Fibrosis stage 3 or 4 was observed in 34%, viral load was high in 77%. Five patients were discontinued for adverse events or on-treatment failure (3 Telaprevir, 2 Boceprevir).

Table 1.

Weeks in therapy	Telaprevir HCV RNA negative (%)	Boceprevir HCV RNA negative (%)
4 weeks (n = 48)	34/36 (94)	2/12 (17)
8 weeks (n = 48)	34/36 (94)	8/12 (67)
12 weeks (n = 48)	34/36 (94)	9/12 (75)
24 weeks (n = 41)	25/29 (86)	9/12 (75)

Among the 15 naive-to-treatment patients, the HCV RNA was undetectable in 93% after 4 weeks of starting telaprevir (or 8 weeks for boceprevir) while it was undetectable in 75% of previous nonresponders or relapsers. Similar response was also observed at weeks 12 and 24. **Conclusion.** Our experience with DAA shows excellent results in non-selected patients is excellent similar to randomized clinical trials. We are monitoring patients for sustained viral response.

PERFORMANCE OF MOLECULAR METHODS FOR DETECTION OF DNA OF HEPATITIS B VIRUS (HBV) AMONG INFECTED INDIVIDUALS

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Purpose. Molecular tests for detection and quantification of HBV DNA are important to determine and to monitore antiviral treatment. In addition, molecular assays are essential for identification of mutations in HBV genome. The objective of this study is to evaluate the performance of four methods (three qualitative and one quantitative) for HBV diagnosis. **Material and methods.** In this study, sera samples from 48 acute or chronic HBV cases without previous treatment and referred to Viral Hepatitis Ambulatory (Fiocruz, Rio de Janeiro, Brazil) were included. Three qualitative methods were evaluated: semi-nested PCR for HBV surface gene (S), PCR for HBV core region (C) and PCR for HBV S region. A commercial quantitative method that amplifies S gene was also employed: Cobas Amplicor HBV Monitor test (Roche Diagnostics, USA). **Results.** Mean age of the participants was 42 years and most of them were male (70.8%). All individuals were HBsAg reactive, 15 presented HBeAg and 17 were anti-HBc IgM reactive. HBV DNA was detected using semi-nested PCR, a PCR for S gene, a PCR for C gene and quantitative method in 89.6%, 60.4%, 47.9% and 87.5% of samples, respectively. HBV mean viral load was 132.361 copies/mL, where 17 samples presented HBV DNA and two were HBV DNA negative by all methods evaluated. **Conclusions.** The semi-nested PCR and commercial quantitative methods were the most efficient for detection and/or quantification of HBV DNA in this study population, and may be used for detection and monitoring of HBV infection.

MONITORING OF THE IMMUNE RESPONSE IN PERSONS VACCINATED AGAINST HEPATITIS B IDENTIFICATION AND NOT RESPONDING VACCINATED WITH INFECTION PRIOR TO THE CAMPAIGN VACCINATION 2008-PERU

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Objectives. To determine titers of anti-HBs in the sample population, percentage of non-responders in vaccinated population, percentage of seroconversion with titles internationally considered non-protective (< 10 mIU/mL). To determine anti HBc in vaccinated as an expression of previous infection **Material and methods.** Design: analytical, observational, prospective study. Population: a representative sample of the total vaccinated between 2 to 19 years old, corresponding to 370 samples. It took participants a venipuncture blood shows about. Titration of anti HBs was performed according to the methodology specified by the laboratory, taking into account the high positive control (> 100 mIU/mL), positive low (< 10 mIU/mL) and negative control to determine the concentrations in each sample. It was proceeded to determine total anti-HBc in the serum of the same patients to search for previous infection **Results.** 370 samples processed in 97.5% (361) were determined protective titers to the vaccine for hepatitis B, 0.81% (3) had no antibodies, 1.08% (4) seroconverted without reaching protective levels. It was achieved to determine 2 cases (0.54%) with infection previous. **Conclusions.** Vaccination protected the 97.5% of the population studied in the protected titles conferred > 100 mIU/mL, post-vaccination time is similar as age > or < 10 years.

RAPID TEST FOR DETECTION OF ANTIBODIES AGAINST HEPATITIS B VIRUS (ANTI-HBS) ARE EFFICIENT TO IDENTIFY IMMUNE INDIVIDUALS?

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Purpose. The objective of this study is to evaluate the efficiency of rapid test for antibodies against HBV (anti-HBs) detection among serum samples. **Materials and methods.** Sera samples from 417 individuals living in Northern Brazil were included and tested for anti-HBs using enzyme immunoassay (EIA) (ETI-AB-AK-3, Diasorin) and rapid test (Imuno-Rápido anti-HBs, WAMA Diagnostics). Both assays employed 100 microliters of sample, however, the average duration of EIA is 4 h and 40 min while rapid test provides results between 15 and 20 min. **Results.** The study population had a mean age (± SD) of 19.5 (± 15.5) years with slight male predominance (51.1%). Anti-HBs marker was detected in 152 samples by EIA with mean titers (± SD) of 136.2 IU/mL (± 220.1). Concordant results between EIA and rapid test were observed in 328 samples, 66 and 262 non-reactive reagents, showing rapid test sensitivity and specificity of 43.4% and 98.8%, respectively. Reactive concordant samples by EIA and rapid test showed the mean (± SD) of optical density to cutoff ratio (OD/CO) equal to 32.45 nm (± 23.15) and mean titer (± SD) antibody equal to 333.3 IU/mL (± 294.3). Highest sensitivity of rapid test was observed among reactive samples presenting antibody titers greater than 100 IU/mL (80.6%). **Conclusions.** Anti-HBs rapid test showed high specificity in comparison to EIA, but the sensitivity of the technique was not as effective, especially among those samples with low values of OD /CO and antibody titers.

CHRONIC HEPATITIS C IN SIX TERTIARY CARE HOSPITALS OF COAST OF PERU: DEMOGRAPHIC AND CLINICAL FEATURES

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Purpose. To describe demographic and clinical features of chronic hepatitis C (CHC) in our region. **Material and methods.** A retrospective case series study in patients with CHC attending Gastroenterology Services at six tertiary referral hospitals of Peruvian coast: five from Lima and one from Trujillo, from September 2011 to February 2012. **Results.** We included 123 patients, 52.8% men. The mean age at diagnosis was 51.47 ± 14.46 years, with 65.8% of cases between 40 and 79 years old. At the time of diagnosis 87% had no symptoms. The serological testing of CHC was performed because of: observation of transaminases' rise (41.5%), high-risk group screening (38.2%), liver related symptoms (17.1%) and screening in health worker (2.4%). Risk factors for viral infection were: Prior major surgery (52%), blood transfusion (37.4%), invasive medical procedures (19.5%), hemodialysis (13.8%), promiscuity (7.3%), health workers, chemotherapy and aspiration drugs (6.5% each), dental procedures and hemophilia (5.7%). We reported HCV/HIV coinfection in 1.6% (n = 2) and HCV/HBV coinfection in 5% (n = 6). At the time of diagnosis 76.4% had non-cirrhotic chronic hepatitis, 18.7% compensated cirrhosis, 2.4% decompensated cirrhosis and 2.4% hepatocellular carcinoma. In the first two groups 40.4% and 26.1% received antiviral treatment. **Conclusion.** In our series, transmission of HCV would predominantly occur in medical centers. Age distribution suggests that transmission is still happening. Diagnosis is mainly related to elevated transaminases with no symptoms associated and at a non-cirrhotic stage. Rate of treatment is still low. It is imperative to improve health processes to stop nosocomial transmission and to optimize early diagnosis and treatment.

IMPACT OF SINGLE NUCLEOTIDE POLYMORPHISMS OF THE IL28B IN TREATMENT RESPONSE OF CHRONIC HEPATITIS C

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Introduction. Recent studies have identified that 2 single nucleotide polymorphisms (SNP) -located on chromosome 19q13- were strongly associated with treatment response in chronic hepatitis C (HCV). SNP rs12979860 C-C has been shown to be an independent predictor of sustained virological response to the treatment with pegylated IFN-α (PEG IFN) and Ribavirin (RBV). On the other hand, SNP rs8099917 G-G has been associated with failure to response. **Objective.** To explore if clinical and humoral factors as well as SNP rs12979860 and rs8099917 are predictive factors of SVR in HCV patients. **Material and methods.** 120 patients with HCV were included in the sample: 66% female; median age of 51.15 years (17-70); 78.3% with genotype 1; 83.3% with HCV RNA level > 400,000 UI/mL; 90% with elevated ALT; 40.8% with METAVIR F3-F4; 35% with hepatic steatosis; 19.2% with history of alcoholism; and treated with PEG IFN α2a-RBV 24/48 weeks. SVR was achieved in 52 (43.3%). DNA was extracted from whole peripheral blood using standard methods. DNA quantification was done by fluorometry and was amplified by PCR, followed by direct sequencing using rs12979860 and rs8099917 nucleotides, both forward and reverse in an automatic sequencer ABI 3730xl. Manual and BLAST analyses were performed on the results against consensus sequence. Statistical analysis. Variables age, sex, HCV genotype, METAVIR stage, viremia level, alcoholism, initial glycemia, SNP rs12979860 and rs8099917, and response to treatment (SVR *vs.* non responders) were analyzed with Medcalc 11.5 program (Chi-squared, Mann-Whitney and student tests) and a multivariate logistic-regression analysis was performed. **Results.** Bivariate analyses showed a significant association with those already known predictive factors of SVR: no history of alcohol or drug abuse; HCV genotype no 1; no cirrhosis; baseline glycemia; and SNP rs12979860 C-C (χ^2 = 6.6; p = 0.0358) and rs8099917 T-T (χ^2 = 8.3; p = 0.0151). The multivariate logistic-regression analysis showed that no cirrhosis, SNP rs12979860 C-C and baseline viremia level < 400,000 UI/mL are independent predictors of SVR (OR = 3.6 IC95 1.5-8.18, OR = 2.7 IC95 1.2-6.2 and OR = 8.07 IC95 2.26-28.72, respectively). **Conclusion.** In patients with chronic hepatitis C, low level of baseline viremia, absence of cirrhosis and SNP rs12979860 C-C are independent predictors of SVR.

CHRONIC HEPATITIS B IN FIVE TERTIARY CARE HOSPITALS OF LIMA, PERU: DEMOGRAPHIC AND CLINICAL FEATURES

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Purpose. To describe the epidemiological and clinical features of chronic hepatitis B (CHB) in tertiary-care hospitals of Lima, capital city of Peru. **Material and methods.** A retrospective case series study of patients with CHB attending Gastroenterology Services of five Limean hospitals from September 2011 to February 2012. **Results.** We included 62 patients from five centers. The average age was 40.46 ± 17.5 years and 59.7% were men. Most had no symptoms at the time of diagnosis (67.7%). Serology tests were indicated for screening in risk groups (35.9%), because of increase in transaminase levels (27.4%), symptoms of liver disease (27.4%) and for blood donor screening (1.6%). Risk factors for virus infection were blood transfusion (25.8%), promiscuity, endemic area and prior major surgery (21% each), prior invasive medical procedures (12.9%), chemotherapy and family members with CHB (11.7% each), health worker and hemodialysis (6.5% each). We found HBV/HIV coinfection in 6.5% and HBV/HCV coinfection in 9.7%. At the time of diagnosis 71% had chronic hepatitis without cirrhosis, 12.9% compensated cirrhosis, 11.3% decompensated cirrhosis and 4.8% had hepatocellular carcinoma. HBeAg-negative variant was majority (53.2%), especially in women (76%) and in endemic area (84.6%). Only 46.8% received antiviral treatment, most at non-cirrhotic stage. **Conclusion.** In our series, patient with CHB living at Lima is predominantly male, forty year old, diagnosed in asymptomatic stages of disease by screening in risk groups or because of transaminase rise. This information would be useful to plan public health programs that enable timely diagnosis and treatment of CHB.

HEPATITIS C VIRUS INFECTION: EPIDEMIOLOGICAL AND CLINICAL EVALUATION A REFERRAL HOSPITAL IN LIMA-PERU

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Purpose. To determine the epidemiological and clinical characteristics of patients with chronic viral hepatitis C (HVCC) at the Hospital Nacional Guillermo Almenara Irigoyen (HNGAI)-Peru. **Material and methods.** A descriptive study of patients diagnosed of HVCC, at HNGAI from January 1998 to September 2009. **Results.** We included 677 patients. The average age was 51.75 ± 16 years and 53.5% were men. Risk factors were: hemodialysis 52.4%; blood transfusions 42%, prior major surgery 23%, health worker 5.7%, chemotherapy, 5.4% and acupuncture or tattoo 1% and sporadic infection 6%. 74% had no symptoms. The initial diagnosis was motivated by: assessments in hemodialysis patients (66.4%), elevated transaminases (15.8%), blood donors screening (9.6%), occupational health screening (6.4%). Liver involvement at diagnosis was: acute hepatitis C in 4%, non-cirrhotic chronic hepatitis C in 72% and liver cirrhosis in 24%. Of the latter, 40% were decompensated. HVCC patients had normal values of transaminases in 42%. We had viral load in 202 patients, 32% had more than 850,000 IU/mL. No differences in the proportion of patients with elevated enzymes or viral load or age, sex, symptoms or need for dialysis. Liver biopsy was performed in 136 patients, 56.6% had fibrosis according to METAVIR. **Conclusions.** Hepatitis C virus infection is a public health problem. This study represents the largest series performed in our country and gives us a close look at the presentation of the disease in our environment, outlining possible targets of action in the planning of primary and secondary prevention of this disease.

USE OF DRIED BLOOD SAMPLES FOR THE DETERMINATION OF VIRAL LOAD, GENOTYPES AND MUTATIONS IN THE CORE-PRECORE REGION OF THE HEPATITIS B VIRUS

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Introduction. The diagnostic and monitoring of the hepatitis B virus infection is routinely done in serum or plasma samples. Dried blood spots (DBS) on filter paper have been used in the diagnostic of several viral diseases due to the advantages in storage and transport to the reference centers. **Purpose.** The aim of this study was to evaluate the utility of the DBS extracted acid nucleic to determine viral load, genotype and mutations in the core-precore (c/p) region of the hepatitis B virus (HBV). **Material and methods.** Transversal analytical study. Forty one patients were included in the study. The serological HBV markers of infection, liver function test, and viral load (VL) were evaluated: the DBS samples were prepared on filter paper cards (S&S903) with 50 μL of blood. They were dried a TA and stored at -20 ºC until use. The VL of paired samples (plasma *vs.* DBS) was measured in the Amplicor Monitor (Roche). The DBS's samples from 10 patients were stored at different temperatures: 4, 25, y 37 ºC for 7 days, and stored at -20 ºC until use. The data was analyzed by Pearson correlation and ANOVA. The DNA extracted from the DBS's and plasma paired samples was purified and a 711 bp fragment from the c/p region of the HBV genome was amplified and sequenced to obtain the HBV genotype and the mutations. **Results.** The analysis of VL data using ANOVA did not show significant difference (p = 0.93) between paired samples stored at different temperatures (IC 95% 2.67-7.83), and a Pearson correlation of 0.94. The PCR amplification of the 711 bp fragment from the c/p region from DBS samples was as efficient as when plasma samples were used. An excellent correlation between the sequences from DBS and paired plasma samples was obtained. The genotype H was the most frequent (97.5%). **Conclusions.** The method validated in this study confirms the utility of the DBS samples because the great advantages for the measurement of VL, genotype identification and molecular analysis of the HBV genome.

FREQUENCY OF OCCULT HEPATITIS B INFECTION (HBVO) IN HIV-1+ PATIENTS FROM MEXICO

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Introduction. Hepatitis B occult infection is characterized by the presence of DNA-HBV in the absence of HBsAg-. Co-infection is frequent in HIV-patients because they share the transmission routes of infection. **Purpose.** The aim of this study was to determine the frequency of HBVO infection in a group of Mexican HIV-1 infected patients. **Material and methods.** Cross-sectional study. Forty nine HIV-infected patients from the Social Security Mexican Institute (IMSS) without HBV infection markers, except anti-HcB, and six HBsAg+ patients were included. Consent informed was obtained. HBsAg, HBeAg, anti-HBc, anti-HBs and anti-HBe levels were determined by EIA, the viral load by Cobas monitor amplicor (Roche), and a quantitative PCR assay (qPCR) was used to confirm the HBVO infection with two genetic markers (X and S) and Syber green, in a LC480 Real time thermocycler (Roche). **Results.** The HBV serological markers showed 47.9% seronegative patients and 52.1% seropositive for HBVO. The frequency of HBVO infection in HIV-1+ patients was high (34.7%). Interestingly, in the seronegative group the 26% had viral loads (< 200 copies/mL). The qPCR results showed a 24.5% of seronegative patients with detectable DNA-HBV for both genetic HBV markers. A 48% (12/25) of seronegative patients had HBVO infection. **Conclusions.** We report a high percentage (52.1%) of anti-HBc+ patients. The frequency of HBVO infection in the group of Mexican HIV-1+ patients is high (34.7%). The qPCR assay was useful to confirm the high prevalence of HBVO infection in HIV Mexican patients.

ARFI ELASTOGRAPHY FOR LIVER FIBROSIS ASSESSMENT IN CHRONIC HEPATITIS C-PILOT STUDY

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Purpose. To evaluate the diagnostic accuracy of acoustic radiation force impulse (ARFI) imaging for the assessment of liver fibrosis in chronic hepatitis C (CHC). **Material and methods.** Prospective pilot study. Included treatment-naive CHC patients (all with PCR HCV RNA +). Other liver diseases were excluded from the study. ARFI elastography was perfor-

med using a Siemens Acuson S2000 ultrasound system. The time interval between liver biopsy (LB) and tissue stiffness was less to six months. Ten ARFI measurements were assessed by the same physician blinded to clinical and biological data. The LBs were assessed according to the METAVIR score by a pathologist blinded to the clinical data and to the results of ultrasound elastography. **Results.** Our study included 29 patients, 16 (55%) male. On LB 06 (20.6%) patients had F0, 07 (24.1%) had F1, 06 (20.6%) had F2, 06 (20.6%) had F3, and 04 (13.8%) had F4. A significant correlation was found between ARFI measurements and fibrosis ($p < 0.001$). For predicting significant fibrosis ($F \geq 2$), for a cut-off of 1.31 m/s, ARFI had 93.7% sensitivity (Se) and 76.9% specificity (Sp) [area under the receiver operating characteristic curve (AUROC) 0.85]. For predicting severe fibrosis ($F \geq 3$), for a cut-off of 1.7 m/s, ARFI had 100% Se and 89.5% Sp (AUROC 0.93). For predicting cirrhosis ($F = 4$), for a cut-off of 2.07 m/s, ARFI had 100% Se and 92% Sp (AUROC 0.95). **Conclusions.** ARFI elastography could identify significant fibrosis, severe fibrosis and cirrhosis with a high degree of accuracy in evaluated patients.

QUANTIFICATION OF HEPATITIS B VIRUS SURFACE ANTIGEN IN PATIENTS WITH CHRONIC INFECTION IN ANTIVIRAL THERAPY: PRELIMINARY REPORT

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Background. Viral load is the most commonly used test to monitor antiviral treatment in chronic hepatitis B virus (HBV) infection. A new method of quantification of the surface antigen of HBV (qHBsAg) using immunoassay, has recently being studied for diagnosis and monitoring the viral replication. This test shows a direct correlation with viral load and intrahepatic cccDNA. In Chile there are no studies done with this test. **Objective.** To evaluate the presence of qHBsAg in patients treated for chronic HBV infection and the relation with their viral load. **Materials and methods.** 154 serum samples of 26 patients on treated for HBV were included. All serum samples were correlated with the clinical data of each patient, such us drug used, response to treatment and viral load. The commercial assay HBsAg II quant on the cobas e 411 platform from Roche diagnostics, was used to measure the qHBsAg. **Results.** In 26 patients, levels of HBsAg and viral load were both elevated before treatment (80.00-450.000 UI/mL) compared to levels during or after treatment (0-170.000 UI/mL), regardless of the drug used. The correlation between viral load and qHBsAg was 52,51% with a p value of 0,00001. In 23 patients (88,46%) this correlation was over 70%. **Conclusions.** qHBsAg shows a high correlation with HBV viral load in patients undergoing treatment against HBV. This new test could be a good alternative to monitor treatment, considering the high cost of alternative molecular tests.

PREVALENCE AND PREDICTIVE FACTORS OF OESOPHAGEAL VARICES IN PATIENTS WITH CHRONIC HEPATITIS C AND PLAQUETOPENIA

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Noninvasive methods for oesophageal varices (OV) diagnosis are increasingly being used in patients with chronic liver disease. Aiming to study the prevalence and the presence of predictive factors of OV, we prospectively evaluated 80 consecutive patients with hepatitis C and plaquetopenia (< 150.000 platelets) never screened for OV by upper gastrointestinal endoscopy (UGE).Patients were submitted to abdominal echography, UGE and had a blood sample for liver function tests. Mean age was 57 years, 50% were male. Ascites was observed in 5%. Liver function was well preserved as evidenced by bilirrubin, albumin and MELD score, 1.4 (± 1.5), 4.4 (± 0.5) and 9.7 (± 3.4), respectively. Most of the patients were classified as Child-Pugh A. Spleen bipolar diameter was 120.7 cm (± 23.4), and 46% had splenomegaly. OV were found in 36% of patients (26% small, 10% large). Patients with OV had higher values of bilirrubin and INR, lower platelet count as well as higher incidence of splenomegaly. On multivariate analysis platelet count was the only independent predictor of OV (AUC ROC 0.72; 95% CI 0.61-0.83; p 0,001). Interestingly, neither spleen diameter, relation spleen/platelets, nor meld or child were independently associated with OV. Patients with platelet count below 50.000, between 50-100.000 and over 100.000 had a prevalence of OV of 100%, 58% and 34%, respectively (p 0,001). The platelets cutoff points with 90% sensibility and specificity for OV presence were 136.000 and 76.000, respectively. **Conclusions.** The degree of plaquetopenia was the only independent factor for the presence of OV in this population.

METABOLIC SYNDROME IN PATIENTS WITH HEPATITIS C: ASSOCIATION WITH HEPATIC FIBROSIS

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Although association between metabolic syndrome (MS) and steatosis has been described, there are few data regarding the relation of MS in patients with hepatitis C to liver fibrosis. We evaluated 232 consecutive patients with chronic hepatitis C submitted to liver biopsy. MS was defined following NHANES criteria. Liver fibrosis was graduated according to Metavir score and considered significant if ≥ 2. Mean age was 52 (± 10) years, 46% were male, genotype 1 and 3 was present in 81% and 18% of patients, respectively. Body mass index was 26.5 (± 4.4), with 64% of overweight and 21% of obesity. Abdominal circumference was 91.1 cm (± 16.4) and 90.0 cm (± 14.4) for males and females, respectively. Serum values of glucose, cholesterol and triglycerides was 106 (± 47), 167 (± 38) and 115 (± 77), respectively. Insulin resistance (IR) was present in 48% of patients. Sixteen percent of patients were diabetic. MS was present in 24% of patients, mostly represented by HAS (45%), low HDL (27%) and high serum glucose (22%). Significant fibrosis was observed in 42% of patients. Steatosis was seen in 47%, and commited more than 30% of the liver sample in 17% of patients. On multivariate analysis the components of MS associated with significant fibrosis were IR (OR 1.93 CI 1.09-3.41) and cholesterol (OR 0.98 CI 0.97 - 0.99). Although associated with MS, steatosis was not associated with significant fibrosis. **Conclusions.** MS is frequent in patients with hepatitis C submitted to liver biopsy. In these patients IR is the only independent predictors of significant fibrosis.

RESISTENCE TO INSULIN AND ADIPONECTIN IN PATIENTS WITH CHRONIC HEPATITIS C WHITOUT MEDICAL TREATMENT

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Purpose. To establish the frequency levels of insulin and adiponectin in patients with chronic hepatitis C without medical treatment (IFNa and ribavirin). **Material and methods.** Insulin, adiponectin and glucose were analyzed, using plasmatic samples with RIA (radioimmunoanalysis) and glucose-oxidase. The results obtained were analyzed in based of case-control study as well HOMA-IR (the homeostasis model for assessment of insulin resistance) set up values to determine the insulin resistance; ≥ 4 indicate insulin resistance and < 4 without resistance. **Results.** 172 subjects were analyzed, 105 men (61%) and 67 women (39%). 92 (53%), patients with chronic hepatitis C (group A) and 80 (47%) healthy people (group B). The insulin average was 27 and standard deviation (SD) 35.4, the glucose average 96 mg/dL SD 12.4, the adiponectin average 11 and SD 8.2. In the case of the group A 18 subjects, 20% of this group, get low values of adiponectin and 65 (71%) HOMA-IR indicates insulin resistance however the group B gets 21% of low adiponectin and 25% insulin resistance. Chronic hepatitis C infection increase 7 times the risk of insulin resistance (RM7.22, IC 95%, 3.67-14.20 p 0.0001). The results prove that low levels of adiponectin is a protective factor in chronic hepatitis C (RM 0.90, IC 95% 0.42-1.89 p 0.85). **Conclusions.** The insulin resistance frequency in chronic hepatitis C patients is 71% whereas in healthy people is only 25%. Results indicate a significant increase level in the chronic hepatitis C patients (OR 7) compared with healthy people. Finally the risk of present diabetes type II increase.

SEROPREVALENCE OF HEPATITIS B AND C, IN BLOOD BANK DONORS FROM A PUBLIC HOSPITAL NETWORK SYSTEM DURING A DECADE IN CHILE (2001-2011)

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Introduction. Hepatitis B and C viral infections (HBV; HVC) are diseases of variable seroprevalence (SP). In Chile there is scant data on this topic. **Purpose.** Communicate the SP of HBC and HCV in blood bank donors (BBD) from Santiago, Chile during a decade, and their distribution according to different age groups and gender. **Material and methods.** The Hospital Salvador Blood Bank Network System (HSBBNS) is the largest in Chile (coverage to 6 Hospitals. All BBD data were included in a computer program. HBV Screening performed by HBsAg (Abbott) and HVCAb by Elisa 3rd generation (Abbott). Since 2007, all HCVAb(+) were confirmed by PCR-RNA. **Results.** Between 2001-2011 the HSBBNS received 178.126 BBD, 63.3% men (n = 112.777), 40% between 18 and 40 years old. The global SP of HBV was 0.034%, and for HVC was 0.47%. The SP of HBV was 0.046% amongst men and 0.012% amongst women (p < 0.05), and for HCV was 0.44% amongst men and 0.52% amongst women (P < 0.05). Only 20% of BBD seropositive for HCV were confirmed as PCR-RNA (+). Both HBV and HVC seropositivity ratio increased as the age of donors increased. **Conclusions.** In our HSBBNS the SP of HBV was 0,034% and for HCV was 0,47% (2001-2011). Only 20% of BBD seropositive for HCVAb were finally PCR-RNA(+). This is a selected population (BBD) without risk factor for hepatitis. The SP of HBV and HCV increases with the age of BBD. The SP of both viral infections if relatively low when compared to other Latin American Countries.

INITIAL "REAL LIFE" RESULTS OF HCV THERAPY WITH BOCEPREVIR IN BRAZILIAN PATIENTS

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Introduction/Purpose. HCV therapy has recently been modified by the inclusion of protease inhibitors (PIs). Restrictive inclusion criteria minimized the experience of dealing with difficult patients (cirrhotic, elderly, previously failed, cytopenics) during pivotal trials. Moreover the population of Latin descent were underrepresented, a fact that becomes even more important "real life" results from Latin America. Recently new Boceprevir's Stopping Rules and early predictive criterias were suggested. Whereas the first generation of IPs will be the best therapeutic option in upcoming years it is essential to quickly obtain data from real life once the life span of the first wave of PIs will be relatively short to allow huge new clinical trials. We present safety and early response data among Brazilians treated with Peg-Interferon/Ribavirin/Boceprevir in real life. **Material and methods.** An observational study of patients (planned 70) with chronic hepatitis C under triple therapy pooled from 4 Brazilians sites. **Results.** Among "null responders" and partial-responders 91% had EVR (10/11) and 7/11 were undetectable at week 8. Among naïves, 4/4 became negative between weeks 4 and 8. Among the patients analyzed 67% (10/15) have advanced disease (F3, F4). No serious adverse events has been reported so far. Compliance have been appropriate. **Conclusions.** So far safety profile is equivalent to Peg-IFN/Ribavirin with significant superiority in terms of EVR. Once confirmed those initial results, the addition of HCV's PIs will dramatically shift the tide of HCV therapy in Latin American patients treated in clinical practice including the so called "difficult to treat".

ASSOCIATION OF TUMOR NECROSIS FACTOR ALPHA AND INTERLEUKIN-10 POLYMORPHISMS ON THE SEVERITY OF FIBROSIS AND LIVER INFLAMMATION IN HEPATOCELLULAR CARCINOMA AND CHRONIC HEPATITIS C PATIENTS

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Purposes. To evaluate the effects of single nucleotide polymorphisms (SNPs) in tumor necrosis factor α (TNF-α) -308 G/A and interleukin-10 (IL-10) -1082 G /A, -819 C / T and -592 C /A promoter genes on the fibrosis and liver inflammation in hepatocellular carcinoma (HCC) and chronic hepatitis C patients. **Material and methods.** We analyzed 52 with HCC and 119 chronic hepatitis C patients. Histopathology of liver was evaluated according to the METAVIR criteria. The HCC was classified according to Barcelona criteria. Genomic DNA was isolated using the Wizard Genomic Blood DNA Isolation Kit (Promega) and SNPs were detected by real time PCR using TaqMan® SNP Genotyping Assays (Applied Biosystems). A multivariate analysis was performed with the backward stepwise method, using SPSS software version 17. **Results.** There was no significant difference between allele and genotype frequencies or between SNPs diplotypes of haplotypes in the IL-10 promoter gene in the evaluated groups. On the other hand, -308 G allele and GG genotype frequencies of SNP TNF-α-308 G/A were significantly higher in patients with HCC compared to hepatitis C patients who had mild fibrosis (p = 0.007 and p = 0.014, respectively) and mild inflammatory activity (p = 0.011 and p = 0.005, respectively). The presence of GG genotype of SNP TNF-α-308 G/A was associated with progression of inflammatory activity in hepatitis C patients with mild activity (p = 0.034). **Conclusion.** The SNPs in IL-10 promoter genes did not influence the degree of inflammatory activity and liver fibrosis. However, TNF-α-308

G allele and GG genotype of SNP TNF-α-308 G/A was more frequent in patients with HCC and it is also related to an aggravation of liver inflammation.

IDENTIFICATION OF CELLULAR PROTEINS REGULATED DURING HCV INHIBITION INDUCED BY ASA USING PROTEOMIC ANALYSIS

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Purpose. We analyzed the proteome of hepatocytes expressing-HCV proteins (replicon cells) treated with ASA to identify cellular proteins involved in the molecular events underlying the inhibition of viral replication. **Material and methods.** Huh-7 hepatocarcinoma cells expressing HCV-nonstructural proteins (genotype-1b) and parental cells were treated with 4mM ASA and harvested at 0-72 h to extract total proteins, which were resolved in 2D gels to separate them by isoelectric point, followed by fractionation by molecular weight. Gels were revealed, scanned and analyzed with PDQuest software. Subsequently, proteins were identified by the pI and PM using TAGIDENT software. **Results.** Proteomic analysis allowed us to determine qualitative and quantitative changes in protein expression profile of HCV-replicon cells treated with ASA. Differentially expressed proteins were identified at 24-72 h post-treatment with ASA. We found that most of the identified proteins that were differentially expressed at 24 h are related to cell proliferation, showing the expression of proteins as MTMR6, FAM22, HDGF and HCF-1. After 48 h, we observed the expression of angiostatin, PI4KA and STAT 1. Finally, at 72 h we identified the adenylsuccinate synthase expression, a protein involved in purine synthesis in the liver and activation of 2', 3'-di-deoxyadenosine protein, as well as ubiquitin-protein ligase E6A, adenylosuccinate lyase and Nibrin (protein related to the viral decrease). **Conclusion.** HCV promotes activation of proteins involved in cell progression, proliferation, inhibition of apoptosis and oncogenesis. This proteomic study allowed us to increase our outlook of the genes involved in the modulation of HCV expression mediated by ASA. Supported by CONACYT-SALUD-2008-01-86-996 and CB2010-01-155082.

INHALATORY SEVOFLURANE CONDITIONING INDUCES HEPATOPROTECTION IN AN EXPERIMENTAL MODEL OF LIVER ISCHEMIA/REPERFUSION INJURY

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Introduction. The pharmacologic preconditioning is strategy applied to increase the tissue tolerance against ischemia/reperfusion (IR) injury. Recently, studies have shown that inhalatory anesthetics may improve I/R injury by an ischemic preconditioning-like mechanism. Postconditioning is a new concept that may have hepatoprotective effect. We aimed to investigate the effects of sevoflurane in experimental warm liver IR injury. **Material and methods.** Fifteen Wistar rats under mechanical ventilation were divided into 3 groups of 5; 1) IR group: rats were anesthetized with intraperitoneal ketamine plus xylazine (standard anesthesia) and submitted to 45 min of warm liver ischemia of the left and median lobes, followed by reperfusion; 2) SEVOPRE group: rats under standard anesthesia were exposed to sevoflurane 2.5% for 15 min, followed by 5 min-washout before 45 min of liver ischemia; and 3) SEVOPREPOST group: rats under standard anesthesia were exposed to sevoflurane 2.5% for 15 min, followed by 5 min-washout before ischemia, plus sevoflurane 2.5% for 15 min at reperfusion. After reperfusion the non-ischemic lobes were immediately removed. MAP was assessed by carotid artery cannulation and mean portal flow (MPF) was by perivascular flowprobe. MAP and MPF were recorded at baseline, 5 min after ischemia, immediately before reperfusion, 5 min and 4 h after reperfusion. AST, ALT, creatinine, pH, bicarbonate (BIC) and base excess (BE), calcium (iCa), potassium (K), glucose and lactate were measured at 4 h postreperfusion. **Results.** AST was decreased in the SEVOPRE (10,056 ± 5,830 U/L) compared to the IR group (16,890 ± 1,630 U/L), $p = 0.018$. ALT was decreased in the SEVOPRE (8,586 ± 5,296 U/L, $p = 0.040$) and SEVOPREPOST (8,956 ± 2,790 U/L, $p = 0.005$) compared to IR group (16,890 ± 1,630 U/L). BIC was increased in the SEVOPRE (12.4 ± 4.4 mmol/L, $p = 0.024$) and SEVOPREPOST (11.2 ± 4.3 mmol/L, $p = 0.049$) compared to IR group (6.7 ± 3.3 mmol/L). BE was increased in the SEVOPRE (-14.72 ± 4.46 mmol/L) compared to IR group (-20.48 ± 4.22 mmol/L), $p = 0.035$. iCa was increased in the SEVOPRE (4.52 ± 0.21 mg/dL, $p = 0.043$) and SEVOPREPOST (4.81 ± 0.23 mg/dL, $p = 0.034$) compared to IR group (3.51 ± 1.47 mg/dL). Serum K was increased in the SEVOPRE (6.30 ± 0.95 mEq/L) and SEVOPREPOST (6.12 ± 1.27 mEq/L) compared to IR group (4.72 ± 0.68 mEq/L). There were no differences in MAP, MPF, pH, lactate, glucose, and creatinine. **Conclusions.** In experimental warm liver I/R injury, sevoflurane conditioning reduced hepatocellular damage demonstrated by lower levels of transaminases, a better acid-base balance and good hemodynamic recovery.

SEROPROTECTION FOR HEPATITIS B VIRUS IN COLOMBIAN ILDREN WITH HIV/AIDS

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Introduction. The seroconversion after vaccination against hepatitis B virus (HBV) is > 90% in healthy children. **Objective.** To determine in children with HIV, the prevalence of seroprotection for HBV and associated factors. **Material and methods.** We included 85 children < 18 years with 3 doses of vaccination, considering clinical, paraclinical, environmental and sociodemographic. Statistical analysis included estimation of the prevalence and associated confidence interval (CI) at 95%, estimated from other descriptive measures of interest and association analysis by multiple logistic regressions. **Results.** 30 children (age 101 ± 44 months) had seroprotection (35.3%, 95%CI 25.2-46.4%). There was no relationship between the seroprotection *vs.* time and dose of vaccination *vs.* no diagnosis and vaccination dose 3. HAART were 89% on average for 5 years. The associated factor was the temporal relationship between vaccination dose 3 and the start of treatment between 0 and 3 years (OR = 4.3; 95%CI 0.96 to 19.23; $p = 0.056$) and > 3 years of onset of treatment (OR = 9.69; 95%CI 2.37 to 39.5; $p = 0.002$). **Conclusion.** > 1/3 of the children showed seroprotection for HBV and was associated with the temporal relationship between onset of treatment and vaccination dose 3.

EFFICACY OF 5 YEARS OF TENOFOVIR DISOPROXIL FUMARATE (TDF) IN CHRONIC HEPATITIS B PATIENTS WITH HIGH VIRAL LOAD (HBV DNA ≥ 9 log^{10} copies/mL)

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Background. TDF is a potent antiviral with activity against hepatitis B virus. Year 4 data demonstrated 97-99% of HBeAg+ and HBeAg- patients on treatment at week (W)192 achieved HBV DNA < 400 copies (c)/mL (69 IU/mL). Whether patients with extremely high baseline levels of viremia respond less well than those with lower viral levels remains unclear. We evaluated the antiviral response over 5 years in both HbeAg- and HBeAg+ patients with markedly high baseline viral load, as defined by HBV DNA ≥ 9 log10 c/mL (8.24 log10 IU/mL). **Material and methods.** 129 chronic hepatitis B (CHB) patients (11 HBeAg- and 118 HBeAg+) with high viral load (HVL) were enrolled across pivotal studies GS-US-174-0102 and GS-US-174-0103 and were randomized to TDF 300 mg (n = 82) or adefovir dipivoxil (ADV) 10 mg (n = 47). After W48, eligible patients (with a W48 liver biopsy) initiated open-label TDF for 7 additional years. On or after W72, patients with a confirmed HBV DNA ≥ 400 c/mL had the option to add emtricitabine (FTC) at the discretion of the investigator. **Results.** Overall, approximately 20% (129/641) of patients enrolled in studies 102 and 103 had an HBV viral load ≥ 9 log10 c/mL. At baseline, the median age of HVL and non-HVL patients was 31 and 43 years, respectively (p < 0.001). 34.9% of the HVL and 53.1% of the non-HVL patients had ALT > 2 x ULN (p < 0.001). 19.0% of HVL and 25.2% of non-HVL were cirrhotic (Ishak 5/6) at baseline (p = 0.148). 91.5% of HVL and 28.9% of non-HVL patients were HBeAg+ at baseline (p < 0.001). There was a similar distribution of patient sex across HVL and non-HVL patients and there was no difference in the distribution of HBV genotypes among HVL and non-HVL patients (p > 0.2 for both variables). At W240, 69.5% of HVL and 83.5% of non-HVL patients normalized ALT (p = 0.010). 2.1% of HVL and 9.5% of non-HVL patients were cirrhotic at W240 (p = 0.093). Among HVL patients who were HBeAg+ at baseline, HBsAg loss was observed in 19.3%, while among non-HVL patients who were HBeAg+ at baseline, HBsAg loss was observed in 4.3% (p < 0.001). **Conclusion.** TDF is highly efficacious in patients with high baseline HBV viral load ≥ 9 log10 c/mL. High rates of HBeAg and HBsAg loss were achieved, and no TDF resistance was observed.

FIVE YEARS OF TREATMENT WITH TENOFOVIR DISOPROXIL FUMARATE (TDF) FOR CHRONIC HEPATITIS B (CHB) INFECTION IS ASSOCIATED WITH SUSTAINED VIRAL SUPPRESSION AND SIGNIFICANT REGRESSION OF HISTOLOGICAL FIBROSIS AND CIRRHOSIS

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Objectives. TDF has demonstrated sustained viral suppression, no resistance, and good safety in CHB patients. We present 5 year on-treatment virologic and paired histology data from studies in HBeAg- (Study 102) and HBeAg+ (Study 103) patients. **Material and methods.** After 48 weeks of double-blind comparison of TDF to adefovir dipivoxil, all patients undergoing liver biopsy were eligible for the open-label TDF extension phase. Subjects were assessed 3 monthly for safety, virology, serology and resistance. Repeat biopsies were performed at year 5 and reviewed by an independent pathologist. **Results.** Of 641 patients randomized and treated, 585 (91%) entered the TDF extension phase; 489 (76%) remain on study at year 5. Paired histologic liver assessments at baseline (BL) and year 5 were available for 348 (54%) patients. 87% showed histologic improvement (M = E); 96% of patients improved or showed no worsening of fibrosis by Ishak scoring, and 74% of cirrhotic patients at baseline had regression of histologic cirrhosis. In multivariable analysis, body mass index (BMI) at baseline was independently associated with regression of cirrhosis (63% in BMI < 26 kg/m^2 and 37% in BMI > 26 kg/m^2; P = 0.0002, OR 9.5 [95% CI, 2.99, 33.04]). At 5 years, 98% of patients on therapy had HBV DNA < 400 copies/mL, and ALT normalization was achieved by 85%, and 73% of HBeAg- and HBeAg+ patients. HBsAg loss (KM%) was observed in 11% of HBeAg+ patients treated with TDF; 1 HBeAg- patient also had HBsAg loss at Week 240. TDF was safe and well tolerated; resistance has not been detected to TDF through year 5. **Conclusions.** TDF remains safe and effective over a 5 year period. These data establish the link between long-term HBV suppression with TDF and regression of advanced fibrosis in the majority of treated patients.

TUBERCULOUS ABSCESS IN THE LIVER AND SPLEEN AS MANIFESTATION OF INMUNE RECONSTITUTION SYNDROME IN A PATIENT WITH AIDS

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A male 36-year old with past medical history of pulmonary TB. Tuberculosis was treated and patient was diagnosed of HIV infection three years ago. He started antiretroviral therapy (HAART) which left it during one year. He referred six months before admission mild abdominal pain, cough and weight loss. He was newly diagnosed of pulmonary tuberculosis AFB (+) in sputum. He started TB treatment with four drugs (INH, RMP, PZA, EMB) and improved symptoms. During the third week of TB treatment, he restarted HAART after which referred increased abdominal pain with high fever and malaise. Physical examination revealed fever, pain on upper abdominal tenderness and visceromegaly. Laboratorial test showed moderate anemia, CD4: 14 cells/mL and test liver function unaltered. An abdominal CT scan showed liver fluid collection in segment I with peripancreatic and retroperitoneal lymphadenopathy. The collection was drained obtaining purulent fluid. Direct smear and cultures for bacterial and fungal was negative. AFB smear and mycobacterial culture was positive and sensitive to all antituberculous drugs. The TB and HAART treatment didn't stop but appeared severe pain in left upper quadrant. A new abdominal CT scan showed a liver abscess and higher splenomegaly with multiple hypodense lesions, so underwent splenectomy. The histopa-

thology showed granulomas with negative AFB and culture positive for *Mycobacterium* tuberculosis. The patient outcome was favorable. **Conclusion.** Tuberculosis should be considered in the differential diagnosis of intraabdominal abscesses in immunosuppressed patients, including in the course of treatment tuberculosis as a manifestation of Immune Reconstitution.

EFFECTIVENESS AT 24 WEEKS OF TENOFOVIR/EMTRICITABINE AND EFAVIRENZ OR LOPINAVIR/RITONAVIR PLUS PEGYLATED INTERFERON ALFA-2B IN HBV/HIV COINFECTED PATIENTS IN MEXICO

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Background. It has been reported in Mexico, genotypes H and G like the most common; in HIV co-infected patients response to treatment of these genotypes is unknown. The aim of the study was to determine the effectiveness at 24 weeks of tenofovir/emtricitabine and efavirenz or lopinavir/ritonavir plus pegylated interferon alfa-2b in HBV/HIV coinfected patients in Mexico. **Material and methods.** We performed a prospective cohort study of patients with HIV/HBV co-infection, HBeAg-positive patients with chronic hepatitis B were assigned to efavirenz 600 mg/daily or lopinavir/ritonavir 400/100 mg twice daily both with tenofovir/emtricitabina 300/200 mg/daily, plus 100 μg/week pegylated interferon alfa-2b for 24 weeks. Patients seen from January 2008 to September 2010 at Hospital de Infectología, La Raza National Medical Center in México City were included. Patients were tested at beginning of study, 4, 12 and 24 weeks after with blood cell count, liver function test, CD4+ cells count, DNA HVB and RNA HIV viral load, HBV serologic panel and genotype test. The study had a primary measure of effectiveness assessed after 24 weeks of treatment-free follow-up: suppression of HBV DNA to levels below 60 IU/mL. Secondary endpoints were HBeAg serocon version (defined by the loss of HBeAg and the presence of anti-HBe antibody) and HBsAg seroconversion (defined by the loss of HBsAg and the presence of anti-HBs antibody). Cumulative incidence and relative risk (RR) with 95% confidence interval (95%CI) were calculated. **Results.** We enrolled 29 men patients. HBV genotypes were F in 3.8%, A in 11.5%, and 42.3% to G and H respectively. The mean (± SD) age was 33.2 ± 7.7 years old. HVB mutations were detected in 20.7% of patients; four patients had M204V mutation and L180M. Median of DNA HBV viral load and RNA HIV viral load were lower at 24 weeks, compared with basal results (300; 1554 *vs.* 853,500; 138,293,250 IU/mL, $p < 0.001$ in HVB and 50; 162 *vs.* 29,400; 183,741 copies/mL, $p < 0.001$ in HIV). CD4+ cells count remained without change (260; 196 *vs.* 178; 309 cells/mL, $p = 0.355$). Primary endpoint was present in 48.2% of patients (95%CI 28.4% - 68.2%) [30% in EFV group and 37.5% in LPV/r; $p = 0.696$]. No differences were observed between patients with and without primary endpoint. Cumulative incidence of loss of HBeAg and HBsAg were 27.6% (95%CI 9.6%-45.6%) and 6.9% (95%CI 0.8%-22.8%) respectively. Patients with one or two secondary endpoints had lower hematocrite (36; 10 *vs.* 43.5; 11.3 mg/dL, $p = 0.021$) lower CD4+ cells count (88; 210 *vs.* 235; 308 mg/dL, $p = 0.019$) and higher glucose (97; 15 *vs.* 88; 10 mg/dL, $p = 0.011$) than those with no one secondary endpoints. Hemoglobin < 12.5 mg/dL (RR 3.28, 95% CI 1.17-9.21) and glucose > 90 mg/dL (RR 2.29, 95%CI 1.25-4.21) were associated to HBV treatment response. **Conclusions.** Tenofovir/emtricitabine and efavirenz or lopinavir/ritonavir plus pegylated interferon alfa-2b is effective in the treatment of patients with HBeAg-positive chronic hepatitis B. Undetectable DNA HBV viral load was obtained in almost 50% at 24 weeks of treatment in H and G genotypes.

PREDICTIVE FACTORS ASSOCIATED TO RAPID VIRAL RESPONSE IN HEPATITIS C VIRUS INFECTED PATIENTS IN MEXICAN POPULATION

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Background. Viral response at 4 weeks of treatment is an important predictor of sustained viral response. The aim of study was to determine the predictive factors associated to rapid viral response (RVR) in hepatitis C virus (HCV) infected patients. **Material and methods.** We performed a cohort study of patients with chronic hepatitis C, who has been subsequently followed during the first 4 weeks of treatment. Patients seen from January 2008 to October 2009 at Hospital de Infectología, La Raza National Medical Center in México City were included. We evaluated 65 chronic hepatitis C (CHC) naive patients who were evaluated to start therapy with PEGylated interferon alpha-2b (1.5 μg/kg per week) and ribavirin (> 75 kg: 1,200 mg and < 75 kg: 1,000 mg). Medical history was recorded for all patients (general attributes, medical problems, and medications), physical exam (height and weight), and laboratory results (blood cell count, liver function test, HCV RNA, and viral genotype). Rapid viral response was defined as negative after 4 weeks of treatment. Statistical analysis was performed with SPSS for Windows (version 12.0; SPSS Inc., Chicago, Ill). Categorical variables were compared using the Pearson's χ^2 or Fisher's exact test. Relative risk (RR) and 95% confidence interval (CI) were calculated to assess the relationship between each risk factor. To adjust for the effects of potential confounders, we used logistic regression models. $P \leq 0.05$ were considered significant. **Results.** We enrolled 26 (40%) men and 39 (60%) women; 45 (69.2%) had HCV genotype 1 and 20 (30.8%) genotype 2 or 3. The mean (± SD) age of our subjects was 48 ± 13.4 years old. Cumulative incidence of RVR was 36.9% (24/65): 20% (9/45) were genotype 1 and 75% (15/20) were genotype 2 or 3; $p < 0.001$. Risk factors associated to RVR were male sex (RR 1.99, 95% CI 1.18-3.57; $p = 0.035$), and genotype 2 or 3 (RR 5.12, 95% CI 2.13-12.33; $p < 0.001$) **Conclusions.** Male sex and genotype 2 or 3 are predictive factors associated to rapid viral response in HCV infected patients in Mexican population.

EL TRATAMIENTO POR DOS AÑOS CON PIRFENIDONA EN PACIENTES CON HEPATITIS CRÓNICA MEJORA LA FIBROSIS, NECROINFLAMACIÓN Y ESTEATOSIS AL REGULAR LA EXPRESIÓN DE LOS RECEPTORES CB1, CB2 Y LOS NIVELES SÉRICOS DE TGF-β E IL-6

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Objetivo. En este estudio se evaluó si el tratamiento durante dos años con el fármaco anti-fibrótico y anti-inflamatorio Pirfenidona (PFD) en pacientes con hepatitis C crónica mejora la necroinflamación, fibrosis y esteatosis mediante la regulación de la expresión génica de los receptores a cannabinoides CB1 (pro-fibrogénico) y CB2 (anti-fibrogénico), así como los niveles séricos de TGF-β, IL-6 y TNF-α. **Material y métodos.** 28 pacientes con hepatitis C crónica recibieron tratamiento con Pirfenidona (1,200 mg/día) durante dos años. Biopsia hepática y muestras de suero se obtuvieron al inicio y al final del tratamiento. La expresión génica en hígado de los receptores CB1 y

CB2 fue valorada mediante PCR en tiempo real. La fibrosis y la necroinflamación se evaluaron por dos patólogos ciegos al estudio utilizando el Índice de Actividad Histológica (HAI) de Knodell e Ishak; la esteatosis se analizó con el programa Image Pro-Plus 5.0. En suero se midieron los niveles de TGF-β, IL-6 y TNF-α con la técnica de ELISA y se realizaron pruebas de función hepática (ALT y AST). El genotipo viral del VHC fue determinado por PCR, la carga viral se midió cada seis meses, y se evaluó la calidad de vida con el cuestionario SF-36. **Resultados.** Al final del tratamiento la fibrosis y la necroinflamación disminuyen en promedio 2 y 3.2 puntos en 67% y 82% de los pacientes, respectivamente. La esteatosis disminuyó de 4.9 a 1.24% en ocho de 13 pacientes. Los niveles séricos de TGF-β e IL-6 disminuyeron significativamente en 93% y 67% de los pacientes, respectivamente; TNF-α disminuyó en 47%. Los receptores CB1 y CB2 se expresaron en todos los pacientes analizados. El RNAm del CB2 se incrementó en 85.7% y el CB1 disminuyó en 28.57% de los pacientes. La ALT disminuyó significativamente en 81% de 91.3 ± 86.6 a 63.8 ± 25.7 UI/mL. El genotipo viral más común fue el 1b. No se observaron diferencias significativas en la carga viral. Finalmente la calidad de vida mejoró en todos los pacientes al final del tratamiento. **Conclusión.** El tratamiento con Pirfenidona disminuye la fibrosis, la necroinflamación y la esteatosis al disminuir los niveles séricos de TGF-β e IL-6 y al regular la expresión génica de los receptores CB1 y CB2 que regulan la progresión de la fibrosis y esteatosis en pacientes con hepatitis C crónica, lo cual contribuye a mejorar la calidad de vida de los pacientes.

ENDEMICIDAD DE HEPATITIS VIRAL B Y BAJOS NIVELES DE CARGA VIRAL EN POBLADORES DE LA COMUNIDAD MATSÉS EN LA AMAZONÍA PERUANA, LORETO 2011

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La hepatitis viral B (HBV) es hiperendémica en comunidades indígenas de la Amazonía Peruana; además de la inmunización, es importante orientar el tratamiento de los portadores crónicos. Se desarrolló un estudio para determinar la prevalencia actual y los niveles de carga viral de la HBV en la población Matsés del distrito de Yaquerana, provincia de Requena en la Región Loreto. **Material y métodos.** Estudio transversal realizado en población general de 14 comunidades de Matsés. Se desarrolló censo poblacional y búsqueda en las cuencas de los ríos y en cada comunidad casa por casa. Se obtuvo una muestra de sangre en la que, mediante ELISA, se determinaron marcadores serológicos de infección para HBV: HBsAg, HBeAg, AntiHBc IgM, AntiHBc total, Anti HBs, Anti Delta, y carga viral mediante PCR en tiempo real. El estudio fue aprobado por el Comité de Ética del Instituto Nacional de Salud y contó con la participación de los dirigentes locales y traductores. **Resultados.** De una población total de 1,556 habitantes se obtuvieron muestras sanguíneas de 965 pobladores, encontrándose una prevalencia total de infección (anti HBc total) de HBV de 36% (348), 3.3% (32) para HBsAg (todos HBeAg negativos), 92% (888) para Anti HBs; en ningún caso se detectaron anticuerpos IgM anti HBc. Todos los portadores de HBsAg eran mayores de 17 años. En la población menor de seis años (129), 92% (888) tuvieron anticuerpos protectores (anti-HBs) y no anticuerpos que indicaran infección pasada (Anti HBc total). 51 personas no presentaron anticuerpos protectores ni marcadores serológicos de infección pasada de hepatitis B, 33.3% de éstos (17) correspondió a niños menores de seis años. De los 32 portadores de HBsAg, la carga viral fue indetectable en ocho; < 6 UI/mL en 16; entre 6-1,757 UI/mL en siete y sólo en uno fue de 3,330 UI/mL. **Conclusiones.** La prevalencia general de infección por HBV es de 36% y la de portadores crónicos 3.32%. En 93% de los casos la carga viral estuvo por debajo de 2,000 UI/mL y sólo un paciente requirió tratamiento, hallazgos que sugieren la necesidad de estudios más específicos orientados a reevaluar el nivel de carga viral como criterio de tratamiento en estas comunidades. En 51 personas (5.2%) no se detectaron anticuerpos protectores contra la hepatitis B, 33.3% de éstos (17) correspondió a niños menores de seis años quienes deben ser inmunizados.

FRECUENCIA DE INFECCIÓN POR VIRUS B Y VIRUS C EN PERSONAL MILITAR DEL EJÉRCITO DEL PERÚ

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Introducción. La prevalencia de hepatitis B (HVB) y hepatitis C (HVC) en el Perú no se conoce exactamente. Diversos estudios indican que sería de 1.7-2% en el caso de HVB y ~1% en HVC. El presente estudio tuvo la finalidad de demostrar la prevalencia de infección por VHB y VHC en una población militar cerrada a nivel nacional y detectar los factores de riesgo relacionados. **Material y métodos.** Se efectuó una encuesta epidemiológica al personal de las diferentes regiones militares de todo el Perú. Se incluyeron oficiales, suboficiales, tropa, personal en retiro y personal civil. En todos los casos se tomaron muestras de sangre para la detección de HBsAg, Anticore total y anti-HVC. Los resultados se analizaron mediante el software SPSS. **Resultados.** Se evaluaron 9,011 personas, la edad promedio fue de 38.11 años. La mayoría de los casos se evaluaron en Lima (67.4%). Predominó la población subalterna (67.73%), seguida por oficiales (31.87%), la población civil fue menos de 0.3%. Como factores de riesgo sólo 3.9% tenía antecedente de hemotransfusión, 0.9% antecedente de consumo de drogas, antecedente de tratamiento quirúrgico 24.4%, antecedente de cirugía menor 13.5%, antecedente de procedimiento médico invasivo 40.9%, varias parejas sexuales 13.3%. En relación con la serología viral, 88 casos tuvieron Anticore positivo (1%), 33 casos HBsAg positivo (0.4%) y 126 Anti-HVC positivo (1.4%). De todos los factores de riesgo analizados únicamente el antecedente de algún procedimiento invasivo tuvo relación significativa con la presencia de infección viral. **Conclusiones.** El presente es el primer estudio epidemiológico de la frecuencia de infección por hepatitis viral B y C a nivel nacional en una población cerrada Se demostró que la infección crónica por VHB es baja (0.4%) y que la de VHC está por encima de lo reportado anteriormente (1.4%), el factor de riesgo asociado a estas infecciones fue el antecedente de procedimientos invasivos, evento que debe alertar acerca de optimizar las medidas de bioseguridad. Si bien es un estudio descriptivo con varias limitaciones, desde el punto de vista poblacional es adecuado para valorar la prevalencia de hepatitis y permitiría hacer una cohorte de seguimiento para analizar la evolución de la hepatitis crónica.

USO DE MEDICINA ALTERNATIVA Y COMPLEMENTARIA EN PACIENTES CON ENFERMEDAD HEPÁTICA EN UNA UNIDAD DE HÍGADO

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Introducción. El uso de Medicina Alternativa y Complementaria (MAC) se ha incrementado de manera significativa en los últimos años. **Objetivo.** Definir el tipo de MAC usada en pacientes hepatópatas de una Unidad de Hígado y describir en el caso de herbolaria, cuál es el principal compuesto utilizado para las enfermedades hepáticas. **Material y métodos.** Se aplicaron 14 preguntas con base en referencias internacionales a pacientes mayores de 18 años, que acudieron a la consulta de la Unidad de Hígado del Hospital Universitario "José E. González" de enero a junio de 2011. Se registraron datos demográficos y nivel de educación; respecto a MAC: frecuencia de uso, costo, categoría de la MAC utilizada, tipo de medicina herbolaria y enfermedad hepática para la que se aplicaba. **Resultados.** Se aplicó la encuesta a 100 pacientes, 13 de primera vez y 87 subsecuentes (60% mujeres y 40% hombres). El 75% eran de región noreste (Coahuila, Tamaulipas, Nuevo León), 19% del centro (San Luis Potosí, Durango, Distrito Federal, Puebla, Veracruz, Guanajuato, Morelos), 4% del sur (Tabasco, Campeche, Nayarit) y 2% de Estados Unidos. Respecto a educación: 38% fueron de nivel superior, 16% de educación técnica, 15% de posgrado, 13% de escolaridad primaria, 11% preparatoria, 6% secundaria y 1% ninguna. El 64% refirió utilizar algún tipo de MAC con la siguiente frecuencia: 33% ocasional, 17% diario, 13% semanal, 1% mensual y 36% refirió ya no utilizarla. El costo invertido por 64% de los pacientes que utilizaron MAC fue menor a 500 pesos en 73%, de 500 a 1,000 pesos en 16%, de 1,000 a 5,000 pesos en 1.6%, mayor a 5000 pesos en 4.7%; ninguno en 4.7%. La proporción en la que los pacientes emplearon al menos un tipo de MAC fue 22%, dos tipos 17% y más de dos tipos de MAC 61%. El tipo de MAC más utilizada fue remedios herbales caseros (90%), seguida por ejercicio o caminata (34%), homeopatía (28%), vitaminas (26%) y acupuntura (25%). De los remedios herbales la manzanilla fue la más utilizada (60%), seguida por la canela (41%), té verde (25%), miel (25%), ajo (20%), hierbabuena (20%). De los remedios herbales para enfermedades hepáticas el áloe vera fue referido en 17%, seguido de cardo lechoso (13%), boldo (5%), diente de león (5%) y gordolobo en 3%. La MAC fue recomendada en 78% de los casos por un familiar o amigo, 6% por un médico de MAC, 5% por internet y 8% por médico alópata. En 3% de los pacientes se presentaron efectos no deseados por el uso de MAC, tales como dolor abdominal y pérdida de peso. **Conclusiones.** El 64% de los pacientes atendidos en esta Unidad de Hígado en un periodo de seis meses utiliza algún tipo de MAC, los remedios herbales es el tipo de MAC más utilizado y el remedio más utilizado fue con base en manzanilla. El áloe vera fue el más utilizado para tratamiento de enfermedades hepáticas.

EL SILENCIAMIENTO DE LA ENZIMA Cu/Zn-SUPERÓXIDO DISMUTASA (SOD1) REVIERTE EL EFECTO ANTIVIRAL DEL AAS EN LA REPLICACIÓN DEL VHC

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Objetivo. Se ha reportado que el VHC causa estrés oxidativo celular mediante la generación de especies reactivas del oxígeno (ROS). Las enzimas antioxidantes, tales como superóxido dismutasa (SOD), catalasa y glutatión peroxidasa, proporcionan una importante línea de defensa contra el daño oxidativo. Previamente nuestro grupo de investigación demostró que el ácido acetilsalicílico (AAS) disminuye los niveles de RNA y proteínas del VHC; sin embargo, el mecanismo es desconocido. El objetivo de este trabajo fue evaluar el efecto de la inhibición de la enzima Cu/Zn-SOD (SOD1) sobre los niveles del RNA-VHC en células Huh7 replicón en presencia y ausencia de AAS. **Material y métodos.** Células Huh7 HCV-replicon fueron transfectadas con siRNA dirigido contra la enzima Cu/Zn-SOD (siRNA-SOD1)(100nM) para silenciar la expresión de la enzima y evaluar su efecto en la replicación del VHC. En paralelo, las células fueron tratadas con AAS 4mM. Posteriormente se extrajo el RNA total a las 24-72 h postransfección, después se sintetizó el cDNA mediante RT-PCR. A partir del cDNA se realizó la qPCR para cuantificar el mRNA-SOD1 y el RNA-VHC, se utilizaron sondas TaqMan específicas. La expresión relativa del VHC se calculó por medio del método $\Delta\Delta$Ct. Se utilizaron actina y GAPDH como genes normalizadores. **Resultados.** Los niveles de mRNA de la enzima SOD1 disminuyeron a 50% aproximadamente a las 48 y 72 h, en las células transfectadas con el siRNA-SOD1 respecto a su control sin transfección a los mismos tiempos. Los niveles del RNA-VHC en células con inhibición de la enzima SOD1 disminuyeron 40% a las 48 y 72 h con respecto a los controles sin transfección. Sin embargo, al combinar la inhibición de la SOD1 y el tratamiento con AAS 4mM, se observó el efecto contrario, el nivel del RNA-VHC aumentó en comparación con los controles sin tratamiento y con las células que se trataron sólo con AAS o inhibidas con siRNA por separado. **Conclusiones.** Se encontró que la inhibición de la SOD1 revierte parcialmente el efecto negativo del AAS en la expresión del VHC. En conjunto, estos resultados sugieren que la actividad de la SOD1 puede determinar la modulación de la replicación subgenómica del VHC en células tratadas con AAS. Este tipo de conocimientos es útil para el diseño de nuevos fármacos antivirales que permitan mejorar el tratamiento de pacientes con hepatitis C. Trabajo subsidiado por CONACYT SALUD-2008-01-86-996 y CB2010-01-155082 otorgado a AMRE.

TEST RÁPIDO DE DETECCIÓN DE ANTICUERPOS ANTI VIRUS HEPATITIS C EN POBLACIÓN QUE CONCURRE A UN HOSPITAL

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Objetivo. El virus hepatitis C (VHC) es una de las principales causas de enfermedad hepática crónica en nuestro medio, pero hay un número indeterminado de sujetos infectados que desconocen su condición. En la celebración del Día Mundial de la Hepatitis se ofreció la detección gratuita de anticuerpos anti VHC a personas que frecuentaban el Hospital Clínico de U de Chile (HCUCH). El objetivo fue estudiar la presencia del anti VHC en una población general de personas que acudían al HCUCH, mediante un test de screening rápido. **Material y métodos.** Se estudiaron todos los sujetos que acudieron en forma voluntaria a realizarse un test de screening rápido (Test card inmunocromatográfico, anti VHC, In Tec, China) que detecta anticuerpos anti VHC en una gota de sangre extraída mediante una lanceta en uno de los dedos de la mano, cuyo resultado se visualiza en 15 min. A todos los sujetos posi-

tivos se les citó y realizó una encuesta, se les investigó los anti VHC por EIA convencional (Axsym Abbott Laboratories, USA) y Carga viral del VHC (TaqMan®, Roche). **Resultados.** Se estudiaron 903 personas, mediana de edad 50 años (rango 2 a 88), 602 mujeres (67%). El 1.7% (15/903) fue positivo para el test rápido y todos se confirmaron con test EIA convencional. El 73% (11/15) conocía su condición de infectado crónico por VHC e incluso 5/11 recibieron terapia antiviral; sólo cuatro pacientes lo desconocía, la carga viral fue positiva solamente en dos de ellos. Los negativos para carga viral presentaron anticuerpos positivos débiles tanto en el test rápido como en el convencional. La mayoría de los pacientes positivos tenía algún factor de riesgo para infección con VHC: siete pacientes recibieron transfusiones sanguíneas, uno tenía tatuaje y dos usuarios de drogas endovenosas (uno de ellos tenía tatuaje). Otros tres tenían cirugía como único factor de riesgo y uno antecedente de esposa infectada con VHC. **Conclusión.** Con el test rápido utilizado fue posible identificar 15/903 sujetos anti VHC positivos (1,7%), test que se correlacionó con la prueba convencional EIA. De los 4/15 sujetos que desconocían su condición de infectados, dos fueron positivos débiles y cargas virales negativas. La mayoría de los casos tenía algún factor de riesgo para la infección con VHC. Este test utilizado por primera vez en nuestro medio fue fácil de realizar y con resultados rápidos, es útil para aplicarse en grandes grupos poblacionales.

RESISTÊNCIA INSULÍNICA EM PORTADORES DE HEPATITE CRÔNICA C NÃO DIABÉTICOS: QUAL O SIGNIFICADO?

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Objetivos. Em portadores de hepatite crônica C não diabéticos, verificar a prevalência de resistência insulínica (RI) e analisar a associação desta com os parâmetros laboratoriais e histológicos. **Pacientes e método.** Foram incluídos no estudo 82 portadores de hepatite crônica C não diabéticos. Exame clínico com determinação da pressão arterial, circunferência abdominal, peso e altura foram obtidos para identificar a presença de síndrome metabólica e cálculo do índice de massa corpórea. Amostras de sangue foram coletadas para determinação de glicose, perfil lipídico, alanina aminotransferase (ALT), aspartato aminotransferase (AST), ferritina, HOMA-IR, carga viral e genótipo do VHC. HOMA-IR superior a 2,5 foi considerado resistência insulínica. Para análise histológica foi utilizada a classificação de Metavir. **Resultados.** A média de idade foi de 51±12,1 anos e 42 (51%) pacientes foram do sexo masculino. Síndrome metabólica e obesidade foram observadas em 24 (29%) e 15 (18%) pacientes, respectivamente. RI foi observada em 27% dos pacientes e foi associada a idade (56.9 ± 10.1 *vs.* 49.7 ± 12.3; p = 0.03), circunferência abdominal (97.8 ± 11.9 *vs.* 87.1 ± 11.1; p = 0.04) e índice de massa corpórea (28.1 ± 4.4 *vs.* 25.4 ± 4.1; p = 0.01). Níveis de ALT, AST, GGT e RNI foram significativamente maiores em pacientes com RI enquanto os níveis de albumina foram menores. Quando comparado a pacientes sem RI, aqueles com HOMA-IR superior a 2,5 apresentaram graus mais acentuados de fibrose hepática e atividade necroinflamatória assim como maior frequência de esteatose hepática à análise histológica. **Conclusões.** É comum a presença de RI em portadores de hepatite crônica C e esta se associa com graus mais avançados de fibrose hepática e atividade inflamatória induzida pelo vírus da hepatite C.

CIRRHOSIS AND COMPLICATIONS

ENDOSCOPIC THERAPY OF GASTRIC VARICES WITH CYANOACRYLATE IN PATIENTS WITH LIVER CIRRHOSIS

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Objective. To evaluate the therapeutic success of the injection of N-butyl-2-cyanoacrylate in the treatment of gastric varices in patients with liver cirrhosis. **Material and methods.** Retrospective study that included 31 patients who only received cyanoacrylate endoscopic therapy between 2006 and 2010. Intravariceally, cyanoacrylate was injected in a 1:1 dilution with lipiodol until the obliteration of varices. The therapeutic situation was: active bleeding, varices with stigmata of recent bleeding and secondary prophylaxis. Treatment success was evaluated according to hemostasis, recurrent bleeding and obliteration. **Results.** Of the 31 patients, 3 (9.7%) were for active bleeding, 18 (58%) with stigmata of recent bleeding and 10 (32.3%) as secondary prophylaxis. Gastric varices were GOV2, 16 (51.6%); IGV1, 14 (45.2%); GOV1, 1 (3.1%). Total hemostasis was achieved in 20/21 (95.2%) and in 2 (66.7%) of 3 patients with active bleeding. Five (16.7%) patients had recurrent bleeding and 2 of them used cyanoacrylate with successful hemostasis. Obliteration was achieved in 24 (77.4%). Five patients died and one for failure of control bleeding. A high severity of Child-Pugh classification was related to treatment endoscopic failure (p = 0.02). The main complication was bleeding after the injection of cyanoacrylate. **Conclusions.** Our results support the use of cyanoacrylate in the treatment of gastric varices with few major complications.

ASSOCIATION BETWEEN LEVELS OF SERUM CREATININE, URINARY CREATININE 24-HOUR, CALCULATED GFR AND MALNUTRITION IN CIRRHOTIC PATIENTS BY DIFFERENT ETIOLOGIES

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Objective. To evaluate the association between the serum creatinine (Cr), urinary Cr 24-h levels, calculated glomerular filtration rate (GFR) and malnutrition in cirrhotic patients by different etiologies. **Material and methods.** Patients with cirrhosis in outpatient follow-up at the Hospital Complex of the Irmandade Santa Casa de Misericórdia de Porto Alegre, Brazil, were evaluated for the nutritional assessment by bioelectrical impedance analysis (BIA) through the phase angle and calculated GFR was achieved by Cockcroft/Gault equation. **Results.** A total of 61 patients were evaluated. The prevalent age group was 60-69 years, which had 20 (32.8%) subjects, followed by 40-49 years, which had 17 (27.9%). Hepatitis C (54.1%) was the most prevalent etiology and was followed by alcohol (32.8%). About the Child-Pugh classification, 38 (62.3%) patients were Child Pugh A, 18 (29.5%) Child Pugh B and 5 (8.2%) Child-Pugh C. Through the phase angle, it was found 19 (31.1%) malnourished patients. The mean serum Cr was 0.99 ± 0.26 mg/dL in malnourished patients and 1.01 ± 0.21 mg/dL in eutrophic (p = 0.688). Significant difference between malnourished and eutrophic in relation to urinary Cr 24-h (p = 0.002), calculated GFR levels (p = 0.044) and GFR classification (p = 0.026) was found. The malnourished

patients had lower levels of urinary Cr 24-h (0.77 ± 0.17 mg/dL *vs.* 1.02 ± 0.44) and calculated GFR (71.6 ± 30.0 *vs.* 87.9 ± 28.1). 26.3% of malnourished had calculated GFR < 50 mL/min while for eutrophic it was 4.8%. **Conclusion.** Malnourished patients had lower levels of serum Cr, urinary Cr 24-h and calculated GFR.

CORRELATION BETWEEN LIPID PROFILE OF CIRRHOTIC PATIENTS, SODIUM AND PROGNOSTIC SCORES

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Objectives. To evaluate the lipid profile (total cholesterol-TC, very low density lipoprotein-VLDL, low density lipoprotein-LDL, high density lipoprotein-HDL, triglycerides-TG) of cirrhotic patients due to alcohol and/or hepatitis C virus (HCV), andto correlate with Child-Pugh score, MELD and Sodium (Na). **Material and methods.** Medical records of cirrhotic patients in outpatient follow-up at Hospital Complex of the Irmandade Santa Casa de Misericórdia de Porto Alegre, Brazil, were reviewed from February to December 2010. **Results.** Medical records of 153 patients were analyzed, of whom 53.6% (82) had cirrhosisby HCV, 32.7% (50) by alcohol and 13.7% (21) by alcohol and HCV. 62.1% (95) weremale and the mean age was 59.3 ± 9.4 years. About the Child-Pugh classification, 46.4% (71) were rated as A, 31.4% (48) as B, and 22.2% (34) as C. As for the MELD, 64.7% (99) had values < 15, 24.2% (37) between 15-19 and 11.1% (17) ≥ 20. It was observedstatistically significant inverse correlation between prognostic scores and lipid fractions. Correlations were found for: Child-Pugh and TC, VLDL, LDL, HDL, TG ($p < 0.001$). MELD and TC, LDL, HDL ($p < 0.001$) and VLDL, TG ($p = 0.030$). Direct correlation, statistically significant, was observed between Na and TC, LDL, HDL, TG ($p < 0.001$), VLDL (p 0.014). **Conclusion.** The decrease in lipid profile was correlated with tools (Child-Pugh, MELDand Na) commonly used to assist in prognosis of liver disease. Therefore, changes in lipidfractions should be considered, since it may contribute to the disease stage.

EFFECT OF MALNUTRITION ON MORBIDITY AND SURVIVAL IN PATIENTS WITH LIVER CIRRHOSIS. CUBAN EXPERIENCE

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Purpose. Liver cirrhosis (LC) is the tenth cause of death in Cuba. The effect of malnutrition on morbidity and survival of patients with LC were investigated in this study. **Material and methods.** 355 cirrhotic patients were included in a prospective study and were followed clinically for 2 year or until death. Child Pugh score was used to assess the severity of cirrhosis. Malnourished were defined when midarm circumference and/or triceps skinfold thickness and/or subscapular skinfold thickness were below the 10th percentile of an age- and sex- matched population. Subjective global assessment (SGA) was used to recorded clinical and nutritional aspects. During follow up 29 patients died. Estimated survival rate was 90.3% at 1 year and 83.1% at 2 years. Multivariate analysis according to Cox's model assessed the predictive power of nutritional parameters on morbidity and mortality. **Results.** Malnutrition was observed in 56.3%.The highest risk was observed in male (OR: 1,9 [IC: 95% 1,2-2,9]), older than 60 years (OR: 1,9 [IC: 95% 1,2-3,0]) and advanced Child Pugh (Child B, OR: 3,7 [IC: 95% 2,2-6,2], Child C, OR:17,4 [IC: 95% 6,0-50,1]). The ethiology of LC was independent of nutritional status. Ascitis, hepatic encephalopathy and spontaneous bacterial peritonitis were more frequent among undernourished. Subjective nutritional elements which better predicted these events were the loss of weight in the last 6 months, dysphagia, vomits and diminished functional capacity ($p < 0,01$). Anthropometrics parameters and SGA results were analyzed as possible predictors of survival. SGA in it's C stage (severely undernourished) ($P < 0,05$) was the stronger independent predictor ($P < 0,05$) as well as Child B and C, hepatocellular carcinoma, hepatic encephalopathy and gastrointestinal bleeding ($P < 0,001$). **Conclusions.** The progression of the illness took into account the commitment of the nutritional state and made a negative influence on survival. The SGA was the best nutritional indicator of survival in LC.

ELECTROCARDIOGRAPHIC ABNORMALITIES IN PATIENTS WITH COMPENSATED AND DECOMPENSATE LIVER CIRRHOSIS WITH ACUTE VARICEAL BLEEDING

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Background & Aims. Cirrhotic cardiomyopathy is a latent chronic cardiac dysfunction in patients with liver cirrhosis and is characterized by myocardial and electrophysiological dysfunction. Several electrophysiological alterations are present, including prolonged QT interval, electro-mechanical dyssinchrony, and chronotropic incompetence. Information regarding the effect of acute variceal hemorrhage on electrophysiological function of the cirrhotic patient is still scarce. The aim was to describe and compare electrophysiological alterations in patients with compensated and decompensated liver cirrhosis from acute variceal hemorrhage. **Material and methods.** Patients 18 years of age and older, with both compensated and decompensated cirrhosis from acute variceal hemorrhage were assessed, and had an electrocardiogram performed. Subjects with chronic renal disease, chronic cardiopulmonary disease, hepatocellular carcinoma, and/or hepatorenal syndrome were excluded. **Results.** The study included 58 patients, with an average age of 56.7 years (±12,9), 39 of which were women; disease etiology was: hepatitis C virus = 34%, autoimmune = 21% and NAFLD = 12%. Child-Pugh score were A = 26%; B = 53%; and C = 21%. Ascites was present in 40%, and 67% was receiving propranolol. Electrocardiogram was abnormal in 60%, with 26% showing more than one alteration, the most frequent being long QT in 45%; no difference was detected between groups. No correlation was found between Child-Pugh and QT interval ($r = 0.035$). Patients with hemorrhage showed abnormalities in conduction (28%) and rhythm (10%). **Conclusions.** Results suggest that electrocardiographic alterations in patients with liver cirrhosis are frequent, regardless of etiology, hepatic reserve and compensation state. In addition, the most frequent alteration is confirmed to be long QT.

RELIABILITY OF LIVER STIFFNESS IN CIRRHOSIS CAN AFFECT ITS ACCURACY FOR CLINICALLY SIGNIFICANT PORTAL HYPERTENSION DIAGNOSIS

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Background. Transient elastography (TE) is an emerging test for clinically significant portal hypertension (CSPH) diagnosis but its reproducibility in liver cirrhosis has not been evaluated. **Aim.** To estimate TE reproducibility in liver cirrhosis and its influence on TE-Hepatic venous pressure gradient (HVPG) association. **Material and methods.** Sixty one patients with liver cirrhosis [HCV, 83%], who received a HVPG measurement for prognosis evaluation (n = 44) or hepatocellular carcinoma treatment (n = 17) were included. After an overnight fast, a single operator performed two consecutive TE measures at different points in the midaxillary line immediately before liver hemodynamic evaluation. Laboratory, clinical and hemodynamic variables were recorded. To evaluate the reproducibility of TE as a continuous variable and as categorical variable (Kp = 13.6, > 13.6 and < 21Kp, Kp = 21), the intraclass correlation coefficient (ICC) and the kappa coefficient (Ki) were used, respectively. Logistic regression identified factors associated with reproducibility. **Results.** Forty-six (75%) patient had CSPH. The HVPG was the only variable associated with reproducibility on multivariate analysis (OR = 1.2, p = 0.005). TE (numerical variable) had excellent reproducibility in the overall cohort, as well as, in patients with or without CSPH. However, it changed across TE stratums (< 13.6 Kp, 13.6-21 Kp, Kp ≥ 21 Kp), decreasing in lower and intermediate levels, as well as the association TE-HVPG. **Conclusions.** TE reproducibility in liver cirrhosis increases with severity, estimate by HVPG but it is not uniform across TE stratum. Decreasing reproducibility in some TE stratums can affect TE-HVPG association.

EVALUATION OF HEPATOPROTECTIVE EFFECT OF HYDROALCOHOLIC EXTRACT OF *ROSMARINUS OFFICINALIS L.* IN HEPATIC ENCEPHALOPATHY WITH CARBON TETRACHLORIDE INDUCED IN THE RAT

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Purpose. In cirrhosis, some toxic substances accumulate in the brain and alter brain function. The extract of *Rosmarinus officinalis L.* has been widely used in various diseases due to its hepatoprotective activity, antioxidant and neuroprotective. In the present study we evaluated the expression of N-methyl-D-aspartate (NMDA) receptor and transporter astrocytic type (GLT-1) in the prefrontal cortex of the rat model of experimental cirrhosis induced with carbon tetrachloride after treatment with *Rosmarinus officinalis L.* **Material and methods.** We used a total of 24 male Wistar rats weighing 80-90 g body weight. We formed three study groups: control group (C) without a treatment, carbon tetrachloride group (CC14), and CC14 group plus *Rosmarinus officinalis L.* (CCl4 + ROM; 1.5 g/kg of extract orally). The treatments were administered three times a week for 8 weeks. **Results.** The expression of the NR1, NR2A and NR2B subunits in cirrhotic animals increased compared to the control group; however treatment with *Rosmarinus officinalis L.* was able to reduce this expression to normal levels compared with CCl4 + ROM groups. While the GLT-1 decreased, but treatment with *Rosmarinus officinalis L.* was able to normalize the expression of both receptor and the GLT-1 with respect to groups of CCl4 and C is an apparent correlation with maintenance of neuronal morphology. **Conclusion.** Treatment with extract of *Rosmarinus officinalis L.* in cirrhotic animals modifies the expression of subunits of the NMDA receptor and GLT-1 due to an improvement in hepatocellular function in the presence of antioxidant compounds and flavonoids.

THE ROLE OF RENIN-ANGIOTENSIN SYSTEM IN THE LIVER FIBROSIS MURINE SCHISTOSOMIASIS

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The major complications of schistosomiasis mansoni are the liver fibrosis development and portal hypertension. The renin-angiotensin system has an anti-fibrogenic effect in several models of liver cirrhosis; however its role on hepatic fibrosis still hasn't been studied. **Purpose.** Evaluate the effect of inhibition of renin-angiotensin system on the hepatic fibrosis in schistosomiasis murine. **Material and methods.** BALB/c mice (n = 40) weighing approximately 20g were submitted to inoculation, route subcutaneous of 50 cercariae, hereafter, were subdivided in three groups: on first group (n = 15), the animals were treated daily with losartan, in dose of 10 mg kg-1 of body weight, intraperitoneally (i.p.), for 12 weeks; the second group (n = 15) was treated daily with lisinopril, in dose of 10 mg kg-1 of body weight (i.p.), for 12 weeks, while the third group (n = 10) was treated daily for amount proportional of solution saline (NaCl 0,9%) (i.p.), equally for 12 weeks. Besides that the animals were sacrificed under anesthesia effect and exsanguinated. To evaluate the progression of schistosomal fibrosis on these animals, were made the following studies on the extracted liver samples: biochemical, histological, immunohistochemical, protein expression, gene expression. **Results.** The treatment with these agents showed a significant decrease of fibrosis murine schistosomal analyzed at the boards stained with Sirius red and of portal hypertension of according with the weight of spleen, where the lisinopril presented best results. For statistical comparisons were applied nonparametric tests of Kruskal-Wallis and of Mann-Whitney, probability values less than 0.05 were considered significant. **Conclusion.** The drugs lisinopril and losartan showed reduction of fibrosis and of portal hypertension on model of murine schistosomal fibrogenesis, however news studies should be carried out to these other mechanisms.

HEPATIC VENOUS PRESSURE GRADIENT (HVPG) IN PATIENTS WITH CIRRHOTIC PORTAL HYPERTENSION AND CORRELATION WITH ESOPHAGEAL VARICES AT ENDOSCOPY

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Purpose. HVPG measurement in cirrhotics with portal hypertension and correlation with esophageal varices at endoscopy. **Material and methods.** We performed 13 HVPG measurements between April 2011 and April 2012. All included patients had portal hypertension evidenced by esophageal varices or splenomegaly. **Results.** 30%(4) of patients had HVPG measure above 12 mmHg, 15% (2) had measure of 10 mmHg and 55% (7) below 10 mmHg. All patients except one with measurement above 12 mmHg had esophageal varices of medium/large size. Among those patients with HVPG below 10 mmHg, all but one had esophageal varices of small size. Patients with red signs had all the HVPG above 10 mmHg. Thrombocytopenia was observed in all patients with HVPG

above 10 mmhg. **Conclusions.** The findings obtained need to be confirmed but there is a tendency of correlation between HVPG above 12 mmhg and large or medium size esophageal varices, HVPG above 10 mmHg and the presence of red signs, which are also associated with bleeding. The gold standard for portal hypertension is HVPG and values above 10 and 12 mm Hg are strong predictors of esophageal variceal formation and bleeding. Thus, further studies are necessary to better document HVPG correlation with varices size.

RELATED FACTORS TO RE-BLEEDING AND MORTALITY IN HEPATIC CIRRHOSIS PATIENTS WITH ACUTE VARICEAL BLEEDING IN HIPÓLITO UNANUE HOSPITAL

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Purpose. To determine the related factors to re-bleeding and mortality at 6 weeks of an episode of variceal bleeding in hepatic cirrhosis patients. **Material and methods.** Descriptive, retrospective, correlational study. They were included hepatic cirrhosis patients who entered to Hipólito Unanue Hospital between January 2006 and February 2012 with suspicion of variceal bleeding. The exclusion criteria were: nonvariceal bleeding, incomplete medical report to determine Child Pugh score, MELD score, or endoscopic report without accurately bleeding source or therapy used. To evaluate related factors to re-bleeding and mortality, we use square Chi test with Yates correction and Fisher test. Data analysis was performed by SPSS 15.0. **Results.** They were enrolled 63 patients. 35 patients were male (55.6%). The median age was 64 years. 26 patients (41.3%) was Child Pugh C, while the median MELD score was 9. The most common cause of hepatic cirrhosis was alcohol intake (31 patients; 39.2%). 53 patients had esophageal variceal bleeding (84.1%) and 26 of them ongoing variceal ligation (49.1%). Univariated analysis found that MELD score was related to re-bleeding before 6 weeks ($p = 0,039$), while Child Pugh score ($p = 0,001$), MELD score ($p = 0,005$), first episode of variceal bleeding ($p = 0.040$) and hemodynamic instability at admission ($p = 0,040$) were related to 6 weeks-mortality. **Conclusions.** MELD score was related to risk of re-bleeding and mortality in hepatic cirrhosis patients with acute variceal bleeding. Child Pugh score, the first episode of variceal bleeding and hemodynamic instability at admission only are related to mortality in our trial.

GASOMETRIC, ECOCARDIOGRAPHIC AND LIPOPEROXIDATION EVALUATION IN EXPERIMENTAL MODEL OF CIRRHOSIS IN RAT

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Introduction. Cirrhosis is characterized by a disruption of hepatic parenchyma associated with the appereance of septs and fibrotic nodules, changes in hepatic blood and risk of liver failure. **Purpose.** To evaluate hepatic, pulmonary and heart alterations caused by the exeprimental model of hepatic cirrhosis induced by intraperitoneal CCl4. **Material and methods.** We used 58 male Wistar rats divided in 8 groups: control group (CO) and other 7 groups divided bu the time of cirrhosis induction by CCl4: G1 (10 weeks of induction), G2 (11 weeks of induction), G3 (12 weeks of induction), G4 (13 weeks of induction), G5 (14 weeks of induction), G6 (15 weeks of induction) and G7 (16 weeks of induction). **Results.** In PaO_2 we found decreased values in groups G2, G6, G7 *vs.* CO ($p < 0,05$), and in pCO_2 the values were found increased in G3 group *vs.* CO ($p < 0,01$), values of AST and ALT were significantly increased in G1 and G5 group *vs.* CO ($p < 0,001$). The liver TBARS values of G1, G3, G4, G6 and G7 groups were found increased when compared to CO ($p < 0,01$) and the lung TBARS values were increased in G5 and G7 groups *vs.* CO ($p < 0,001$). In echocardiography we observed decreased values of the posterior wall in diastole in groups G1 and G5 *vs.* CO ($p < 0,01$ and $p < 0,05$) and in the anterior wall, systole and diastole values were decrased in G1, G5 and G7 groups *vs.* CO ($p < 0,05$). **Conclusion.** The induction of CCL4 caused cirrhosis, besides causing alteration in gas changes and altering the structure of the heart wall.

STRUCTURAL ASPECTS OF TASTE BUDS AND ANALYSIS OF CELL CAPACITANCE BY BIOELECTRICAL IMPEDANCE ANALYSIS OF CIRRHOTIC RATS

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Introduction. The protein-caloric malnutrition in cirrhotic patients is well documented in various clinical trials, ranging from 10% to 100% of cases. This discrepancy in the nutritional diagnosis occurs because currently there is no capable instrument for characterizing the nutrition of these patients. Bioelectrical impedance analysis (BIA) has showed to be a possible method of nutritional prognosis by using the cell capacitance (CC) through the phase angle (PA). This nutritional deficit is due to many factors, being the dysgeusia the most commonly reported complaint. Ethical considerations limit procedures in human beings, so animal models are appropriate.**Objetives.** To analyze the taste buds of cirrhotic rats, identifying possible changes in histolology (HE), scanning electron microscopy (EM) and to evaluate the CC through the BIA. **Material and methods.** We used 30 male Wistar rats (± 250 g) from FEPES. The animals were divided into 1 - (CO) received intraperitoneally (ip) 0.9% NaCl, and 2 - (DEN) received ip diethylnitrosamine (DEN-50 mg/kg) 2x/week and water plus phenobarbital (0.3 g/L) ad libitum. In order to evaluate the CC, one hour after the first application of DEN, BIA was performed. At 10 weeks the animals were killed and the tongue removed for histological analysis by HE staining. For morphological analysis, ME. **Results.** Values of AF in group 2 had an average of 5.79° (±1.25) and CO 7.39° (± 0.99) ($p \leq 0.001$). The liver function tests in group 2 compared with CO showed significant differences ($p \leq 0.001$). Histologically there is no difference between the groups. The ME data showed changes in morphology between the groups where in wich we could identify a group DEN with flattening of taste buds. **Conclusion.** The AF showed changes in functionality of DEN group, along with liver dysfunction. There are significant structural changes of taste buds in the DEN group.

CORRELATION OF SERUM CA-125 ANTIGEN WITH THE CHILD PUGH CLASSIFICATION IN PATIENTS WITH LIVER CIRRHOSIS

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Purpose. Serum cancer antigen (CA) 125 elevation has been reported in patients with liver disease, but it is poorly charac-

terized. Our objective was to determine whether there is correlation of serum CA-125 antigen with the degree of hepatic functional reserve, according to Child Pugh Turcotte classification in cirrhotic patients. **Material and methods.** Were recruited 92 patients diagnosed with cirrhosis of different etiologies. 40 patients (43.5%) met the inclusion criteria, 28 women (70%) and 12 men (30%) whose ages ranged between 41 and 60 (57.5%) were included in the study. Physical examination, laboratory, ultrasound and CA-125 dosage were performed the same day. With the results, we grouped patients according to Child Pugh Score: 5 patients with grade A (12.5%), 21 patients with grade B (52.5%) and 14 patients with grade C (35%). **Results.** The mean serum level of CA -125 for patients with Child-Pugh grade A was 27.51 IU/mL, for grade B was 169.68 IU/mL and for grade C was 725.40 IU/mL. In analyzing the nonparametric correlation coefficient showed that there was a linear association between two variables, with statistical significance ($p < 0.000$). In linear regression analysis, the value of R2 was 0,518 found a moderate relationship between both variables and also a regression coefficient or slope of line 0004. **Conclusions.** Elevated CA-125 antigen is common in cirrhotic patients regardless of etiology. There is a direct correlation with Child-Pugh Score, which could help us make it more objective to measure the degree of liver dysfunction in cirrhotic patients.

NUTRITIONAL EVALUATION AND AGREEMENT BETWEEN METHODS OF ASSESSMENT IN THE CIRRHOTIC PATIENT

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Malnutrition is a prevalent problem in our cirrhotic population that conditions an additional risk for infections leading to increased morbidity and mortality in these patients. The real prevalence of this problem is unknown in our country and the intervention is not effective unless you consider the basic nutritional diagnosis. For this reason this study aims to determine the nutritional status of hospitalized cirrhotic patients through different methods of assessment and set up the degree of concordance between them. **Material and methods.** We included 91 cirrhotic patients hospitalized in the Department of Liver of Hospital Edgardo Rebagliati - Lima-Peru from June 2011 to January 2012, which underwent nutritional assessment by Subjective Global Assessment (SGA), anthropometry and body mass index (BMI). For Anthropometry there were considered: weight, height, arm circumference and triceps skinfold, measured by the physician and nutritionist. The triceps skinfold was obtained through a caliper on the back of the right arm (or dominant arm), at the midpoint between the olecranon and the acromion. At that point there was also measured the arm circumference. **Results.** Mean age was 61.8 years (range 23-92), 60% were male (55 patients), distributed as follows: 36% Child A (33 patients), 42% Child B (38 patients) and Child C 22% (20 patients). 41% of the population had ascites (37 patients) and we found 33% of Malnutrition by SGA, 33% of malnutrition by anthropometry and only 3.3% of malnutrition by BMI. Both VGS as anthropometry malnutrition were greater at higher Child stage (Child C: 75% by VHS and 70% by anthropometry). We set up an adequate correlation between VGS and Anthropometry but not with BMI. **Conclusions.** The frequency of malnutrition in our population was 33%, assessed both by anthropometry and VGS, methods that had adequate agreement. Malnutrition is more prevalent with advancing deterioration of liver function assessed by the Child.

NUTRITIONAL ASSESSMENT IN PATIENTS WITH CIRRHOSIS. HOW SHOULD THESE PATIENTS BE EVALUATED?

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Purpose. i) To estimate the nutritional status with SGA and OA and the concordance between both methods in patients with cirrhosis. ii) To establish if a poor nutritional status is associated with more advanced cirrhosis and the relationship between cirrhosis etiology and PCM. **Material and methods.** 168 outpatients and inpatients were included in the sample: 60.7% female; median age of 60.6 ± 12 years; and diagnosed cirrhosis, between May 2009 and October 2010. In all of them SGA and OA were performed. Patients with hepatocellular carcinoma or other tumors and HIV infection were excluded. Statistical analysis: i) Variance (ANOVA) and Chi-squared tests. ii) Concordance weighted kappa coefficient between SGA and VO. **Results.** Etiology of cirrhosis was viral (HCV/HBV) in 67 (39.9%), alcoholic in 29 (17.3%), cryptogenic in 22 (13.1%), autoimmune in 19 (11.3%), primary biliary cirrhosis in 15 (8.9%) and other causes in 16 (9.5%). Child Pugh's class A cirrhosis was observed in 63.7% and MELD < 15 in 84.5%. The risk of malnutrition (MR) or malnutrition (M) was 69.7% when patients were evaluated with SGA (29.8% with severe malnutrition –SM-) and 48.8% with OA (8.4% SM). Alcoholic patients had SM in 58.6% (SGA) and 30% (OA). This finding was significantly superior when compared to the other etiologies ($p = 0.002$ and $p = 0.001$, respectively). The concordance between SGA and OA was low (Kappa = 0.30 - CI95 0.20-0.40). OA showed MR or M in 41.5% Child Pugh's class A patients (SM in 1.8%), 56.8% (SM 11.3%) in class B and 72.2% in Child Pugh's class C. Using Child Pugh and MELD scores, the stage of cirrhosis was found to be correlated with OA ($\chi^2 = 21,4$; gL = 4;$p = 0,0003$ and $F = 6,32$; $p = 0,002$) as well as with SGA ($\chi^2 = 53,5$; gL = 4; $p < 0,0001$ and $F = 28,3$; $p < 0,001$). SM with both SGA and OA was significantly superior in patients with Child Pugh's class C and MELD >15. **Conclusion.** Even though in this group of patients with cirrhosis the concordance between SGA and OA was low, malnutrition –with both methods– was observed in an elevated percentage of cases. In alcoholic patients malnutrition was even more frequent. There is a strong correlation between the grade of malnutrition and both Child Pugh and MELD scores.

EPIDEMIOLOGY, CLINICAL FEATURES AND SHORT-TERM SURVIVAL IN PATIENTS DIAGNOSED WITH LIVER CIRRHOSIS AT THE HOSPITAL CAYETANO HEREDIA

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Objective. Determine the epidemiology, clinical features and short-term survival in patients with liver cirrhosis hospitalized since October 2011-October 2012 at the Cayetano Heredia Hospital. **Materials and methods.** Studio transversal, observational, descriptive. This includes all patients diagnosed with liver cirrrosis hospitalized, age over 18 years, between the months of October 2011 to October 2012. All those elected were followed for six months after hospital discharge. **Results.**

We identified 67 patients diagnosed with cirrhosis, 40 women and 27 men, average age was 57 years. Etiology: chronic alcoholism in 44% (30 patients), probable NASH in 22% (15 patients), viral in 15% (6 patients with HCV and HBV 4 patients), unspecified 10% (7 patients). The severity according to Child Pugh classification was C in 61% (41 patients), B in 28% (19 patients) and A in 14% (10 patients). The main reasons for hospitalization included encephalopathy (30%), variceal bleeding (28%), infection (28%) and ascites (7%). Complications most often identified during hospitalization was infection (NIH). Hospital readmission during follow-up encephalopathy (11%) and variceal gastrointestinal bleeding (5%). Survival at six months is 40% (13/32 patients). **Conclusion.** Cirrhosis affects women in greater proportion and are chronic alcohol consumption and NASH probably the main causes. Encephalopathy and gastrointestinal bleeding are the main reasons for hospitalization. Most of the patients have advanced stage disease. The most frequent infections are spontaneous bacterial peritonitis and pneumonia. Of the patients with short follow-up made less than 50% will survive.

IMMUNE RESPONSE INVOLVEMENT IN ALCOHOLISM AND ALCOHOL LIVER INJURY

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Purpose. To evaluate in peripheral blood lymphocyte profile of patients with chronic alcoholism and its relation to alcohol liver disease (ALD). **Material and methods.** Two groups of patients of the liver clinic in the General Hospital of Mexico were studied; the first one integrated by subjects with alcoholism criteria without ALD, the second one for subjects with any grade of ALD and a control group was included. The lymphocyte profile was determined (T lymphocytes, NK cells, NKT cells, B lymphocytes, TCD8 and TCD4 cells) in peripheral blood by flow citometry. ANOVA test and orthogonal analysis were used for the statistic analysis. **Results.** 129 subjects were included, of which 66 were controls, 53 had alcoholic liver injury and10 were chronic alcohol consumers. The mean age (years): 39 ± 10, 49 ± 13 and 45 ± 16 respectively, only finding differences between control group and the other two groups ($p = 0.014$). Difference was found in the subpopulation values of T lymphocytes, NK cells and NKT cells between patients with and without ALD versus control group ($p = 0.007$ and $p = 0.010$ and $p = 0.04$ respectively). Also T lymphocyte and NK cells were statistically different between the control group and group without liver injury ($p = 0.032$ and $p = 0.010$ respectively). **Conclusions.** We found differences in T lymphocytes, NK and NKT cells between controls and alcoholics (with and without liver injury). The differences in NK cells and T lymphocytes between the control group and the group without liver injury suggest that immune alterations are present since subclinical stages of alcohol liver disease.

EVALUATION OF OXIDATIVE STRESS THROUGH THE RATIO OF REDUCED/OXIDIZED GLUTATHIONE IN ALCOHOL LIVER DISEASE

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Purpose. To study the concentration reduced glutathione, oxidized and GSH/GSSG ratio in alcoholic patients with ALD. **Material and methods.** We included 64 patients with ALD consulting the General Hospital of Mexico with alcoholism according to WHO criteria (> 70 g/day in men, > 50 g/day in women for 5 years). The control group (CT) consisted of 66 teetotalers or alcohol consumers of < 10 g per day and AUDIT < 5. Blood samples were taken in one occasion (3 mL) for determination of GHS and GSSG (Calbiochem, USA). We obtained written informed consent each subject. T-test was use for statistical analysis. **Results.** We included 66 CT, mean age was 39±9 years and body mass index (BMI) = 28 ± 3 kg/m^2. Also were included 64 ALD with a mean age of 49 ± 13 years, BMI = 28 ± 4 kg/m^2. The average grams of alcohol/day for CT = 2 ± 2 g while group ALD = 308 ± 208 g, mean years of consumption was 28 years. GSH concentration (μM) in CT was 516 ± 133, in the case of ALD was 807 ± 170 ($p < 0.001$). The concentration of GSSG (μM) was CT = 179 ± 172 and ALD = 321 ± 386 ($p = 0.020$). The value GSH/GSSG ratio for CT was 3 ± 3 and the ALD of -9 ± 3 ($p < 0.001$). The ratio was lower in ALD when compared with CT. The GSH/GSSG ratio is an indicator of oxidative stress. **Conclusion.** This is the first study to be performed with ALD. We found high concentrations of GSH and GSSG while the ratio was lower. This study confirms that the concentration of GSH, GSSG and GSH/GSSG ratio participate in alcoholism and ALD, the determination of these molecules could improve the diagnosis and treatment of patients with this damage.

EPIDEMIOLOGICAL CLINICAL PROFILE OF LIVER CIRRHOSIS IN LIMA-PERU

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Purpose: To determine the epidemiological, clinical, laboratory, endoscopic and ultrasound characteristics for patients with liver cirrhosis of the hospitals in Lima. **Material and methods.** It is an observational, descriptive, transversal, prospective study of case series. The study was conducted in 2011. We included patients over 18 years of age, clinical and/or histological diagnosis of cirrhosis of the liver, from 12 hospitals in Lima, Peru. **Results.** We included 302 patients, mean age was 64.05 years and the distribution according to sex was: male 170 (56.29%) and female 132 (43.71%). The most common etiologies were alcohol (27.48%), NASH (12.91%) and viral hepatitis C (10.92%). The most common findings on physical examination were: telangiectasis (53.97%), liver Palmas (49.33%), ascites (40.72%) and hepatic encephalopathy (29.47%), distribution according to the severity of hepatic encephalopathy was 6.95% I, 14.56% II, 7.61% III and IV 0.66%. Abdominal ultrasound was suggestive of liver cirrhosis in 61.58% of cases and portal hypertension in 37.08% of cases. Esophageal varices were diagnosed in 42.71% of the population studied and gastropathy hypertensive patients in 15.52%. The main reasons for diagnostic were upper gastrointestinal bleeding (20.52%) and ascites (16.88%). The distribution according to Child-Pugh Score was A (10.92%), B (53.64%) and C (20.86%). The average MELD score of the study population was 12.84 ± 5.44. **Conclusions.** The cirrhotic patients studied showed advancing age, male predominance and an intermediate degree of liver dysfunction. The main reason for diagnostic was upper gastrointestinal bleeding.

EFECTO DEL EXTRACTO DEL *ROSMARINUS OFFICINALIS L.* SOBRE LAS ALTERACIONES COGNITIVAS EN UN MODELO DE ENCEFALOPATÍA HEPÁTICA EN LA RATA

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Introducción. La cirrosis hepática es una causa común de muerte en el mundo, una de sus principales complicaciones es la encefalopatía hepática, caracterizada por el aumento en la concentración de sustancias tóxicas, como el glutamato extracelular que se acumula en el cerebro, que alteran la funcionalidad cerebral. La estimulación excesiva de receptores a glutamato tipo NMDA permite el influjo de Ca2+ a la célula postsináptica e induce a la activación de vías de señalización y muerte neuronal. Las estructuras más vulnerables al daño excitotóxico son el hipocampo y la corteza cerebral prefrontal (CCPF) que resultan indispensables para el adecuado desarrollo de diferentes capacidades cognitivas como la orientación espacial (OE), el pensamiento lógico-matemático, la planeación y la organización de la memoria de corto plazo (MCP). **Material y métodos.** En el presente trabajo se evaluó el efecto del *Rosmarinus officinalis L.* en un modelo de daño hepático inducido con tetracloruro de carbono (CCL4) en ratas Wistar tratadas con extracto de *Rosmarinus officinalis L.* a dosis de 1 g/kg una semana antes y durante la intoxicación crónica con CCL4. Al término del tratamiento se evaluó la MCP con el laberinto de Biel de piso firme y la OE con el laberinto acuático de Morris. **Resultados.** Las ratas con daño hepático mostraron alteraciones en el desempeño de una prueba de MCP y OE, lo que estaría ligado a la disfunción de la actividad neuronal del hipocampo y la CCPF. **Discusión.** El efecto observado del extracto de *Rosmarinus officinalis L.* quizás se deba al restablecimiento de la función hepatocelular y como consecuencia al restablecimiento del metabolismo del glutamato. **Conclusión.** El tratamiento con el extracto de *Rosmarinus officinalis L.* mostró un efecto protector. Sin embargo, estudios adicionales son necesarios para evaluar la expresión del transportador a Glutámico GLT-1 y de las subunidades NR1, NR2A y NR2B del receptor tipo NMDA, así como medir la actividad de las enzimas implicadas en el ciclo de la urea y aminoácidos aromáticos que permitan esclarecer el mecanismo exacto de la acción de *Rosmarinus officinalis L.*

CONDIÇÃO FUNCIONAL, FORÇA MUSCULAR RESPIRATÓRIA E QUALIDADE DE VIDA EM PACIENTES CIRRÓTICOS

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Introdução. As doenças hepáticas são responsáveis por alterações metabólicas e musculares, que interferem negativamente na qualidade de vida desses pacientes. **Objetivo.** Comparar a condição funcional, força muscular respiratória e qualidade de vida (QV) nos pacientes cirróticos conforme as etiologias: vírus da hepatite C (VHC), vírus da hepatite B (VHB) e cirrose por álcool (CA) e correlacionar o teste da caminhada dos seis minutos (TC6min) e a força muscular respiratória com o Model for End-stage Liver Disease (MELD). **Materias e métodos.** Estudo transversal, composto por 86 pacientes: VHC (n = 40 pacientes), VHB (n = 14 pacientes) e CA (n = 32 pacientes). **Resultados.** O grupo CA apresentou menor distância no TC6min, quando comparado, respectivamente, aos grupos VHB e VHC; 373,50 + 50,48 (m), 464,16 + 32,00 (m) e 475,94 + 27,84 (m), p = 0,001. No SF-36, o grupo CA apresentou menores escores na capacidade funcional e limitações de aspectos físicos, quando comparado aos grupos. A força dos músculos respiratórios, o grupo CA apresentou menor PImáx, quando comparado com os grupos VHB e VHC; -65,54 + 11,28(cmH2O); -71,61 + 6,96 (cmH2O); -82,44 + 13,71(cmH2O), respectivamente, p = 0,001. Na comparação da PEmáx, o grupo CA obteve menores valores do que os grupos VHB e VHC; 65,13 + 10,74 (cmH2O); 82,44 + 13,87 (cmH_2O); 83,44 + 12,20(cmH2O), respectivamente, p = 0,001. Na correlação do MELD com o TC6min, houve forte correlação inversa r = -0,74, p = 0,0001, MELD *vs.* PImáx, r = - 0,55, p = 0,0001. **Conclusão.** O grupo CA apresentou: pior condição funcional; força muscular respiratória e qualidade de vida que os pacientes com VHC e VHB.

A CAPACIDADE FUNCIONAL, FORÇA MUSCULAR INSPIRATÓRIA E O CONSUMO MÁXIMO DE OXIGÊNIO PREDIZEM A MORTALIDADE EM PACIENTES CIRRÓTICOS

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Introdução. As manifestações sistêmicas das doenças hepáticas crônicas repercutem negativamente nas funções músculo-esqueléticas, no qual interfere negativamente na capacidade de exercício dos pacientes cirróticos. **Objetivos.** Verificar o Teste da Caminhada dos Seis Minutos (TC6min), Força Muscular Inspiratória (PIMáx) e a capacidade máxima de exercício (VO2) na sobrevida de pacientes cirróticos. **Materiais e métodos.** Coorte prospectivo (3 anos) , composto por 86 pacientes que possuíam o diagnóstico de cirrose hepática através das etiologias: vírus da hepatite C (HCV), vírus da hepatite B (HBV) e cirrose alcoólica (CA). **Resultados.** Na análise da sobrevida, os indivíduos que obtiveram a distância percorrida do TC6 min < 410 m apresentaram sobrevida de 55% *vs.* 97% quando comparados com aqueles > 410 m, p = 0,0001, risco relativo 4,21, IC 95%. Em relação à PImáx, os indivíduos que ficaram abaixo de -70 cmH2O apresentaram sobrevida de 62% *vs.* 93%, quando comparados com aqueles acima de -70 cmH2O, p = 0,0001, risco relativo 2,25, IC 95%. Na comparação do VO2 aqueles que obtiveram valores abaixo de < 17 mL/kg/min apresentaram sobrevida de 55% *vs.* 94% quando comparados com valores > 17 mL/kg/min, p = 0,0001, risco relativo 4,10, IC 95%. Quando realizamos a análise de sensibilidade e especificidade através da curva ROC, o TC6 min, VO2 e PImáx apresentaram valores de área acima de 0,70 e boa sensibilidade e especificidade em relação a mortalidade. **Conclusão.** A distância percorrida no TC6 min, PIMáx e o consumo de oxigênio são variáveis preditoras de mortalidade em pacientes cirróticos.

EXPERIMENTAL HEPATOLOGY

VITEX AGNUS CASTUS REVERSES THE HEPATIC STEATOSIS IN AN ANIMAL MODEL OF ESTROGEN DEFICIENCY

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Aims. *Vitex agnus castus* is a plant that has been used as an alternative form in the treatment of the symptoms of menopause. The aim of this study was to evaluate the effects of *Vitex* on the hepatic lipid metabolism, in an animal model of estrogen deficiency associated with HS. **Material and methods.** Eleven weeks after the surgical procedure of ovary removal, ovariectomized (OVX) Wistar rats were treated with daily doses of *Vitex* dried fruit extract (Agnoside®, 1.6 mg/kg), over a period of 15 days. Then, the liver lipid contents and capacities of oxidizing fatty acid by isolated mitochondria and peroxisomes as well as the liver redox status were evaluated. The plasma lipid profile and the glicemia were also assessed. **Results.** The development of HS was prevented in OVX rats treated with *Vitex* (OVX + VA), which also presented lower plasma levels of triacylglycerols (TG) and VLDL-cholesterol. However, these effects could not be attributed to improvement in the liver capacity of fatty acid disposal by peroxisomal or mitochondrial β-oxidation pathways. The liver glutathione contents and the activity of glucose 6-phopshate dehydrogenase (G6PD), both reduced in OVX rats, were restored in OVX + VA rats. **Conclusion.** *Vitex* prevented the development of HS, a phenomenon that could be a result of an inhibitory action of this extract on the hepatic synthesis of lipids, as suggested by the reductions in the plasma levels of VLDL-cholesterol and TG. *Vitex* also restored the activity of G6PD and the liver contents of GSH.

HORMONAL RESUSCITACION THERAPY (METHYLPREDNISOLONE+TRIIODOTHYRONINE) IN ISOLATED PERFUSED RAT LIVER

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Purpose. Hormonal resuscitation therapy before trasplant, specifically administration of methylprednisolone (MP) and thyroid hormone (T_3), improves the conditions of cardiac graft, but the impact over other organs is not clear. We study the effects of MP+T_3 in the isolated perfused rat liver system, evaluating Küpffer cells activation and organ damage by histology. **Material and methods.** Male Sprague Dawley received a single injection of MP (34 mg/kg), T_3 (0,05 mg/kg) and/or equivalent volumes of vehicle (vMP or NaOH) prior laparotomy. Liver was perfused *in vitro* via the portal vein in a non-recirculating system during 45 min. Colloidal carbon (CC) 0.5 mg/mL was infused the last 15 min of perfusion. Oxygen consumption was determined in the effluent perfusate with a Clark-type O_2 electrode continuously. At the end of perfusion, tissue samples were fixed in 10% buffered-formalin, paraffin embedded, and sections were stained with hematoxylin-eosin for histological studies. **Results.** CC infusion increased the rate of hepatic O_2 consumption over basal values in all but vMP + NaOH group (MP + T_3 = 0.316 ± 0.04; MP = 0.362 ± 0.04; vMP = 0.3 ± 0.04; T_3 = 0.15 ± 0.0, NaOH = 0.04 ± 0.01 μmol O2/g liver/min). The uptake of CC showed a linear relationship as a function of the time of carbon infusion. Histological assessment of studies revealed normal architecture and pericentral liver injury in all groups, with decreased injury areas in MP+T_3 (15% of total area), MP (35%) and T_3 (45%). **Conclusions.** Administration of hormonal resuscitation therapy maintains the functional capacity of Küpffer cells reflected in liver O_2 consumption, while minimizing reperfusion organ damage evaluated by histology.

HEPATOPROTECTIVE EFFECT OF *SPIRULINA MAXIMA* ON STREPTOZOTOCIN-INDUCED DIABETES IN RATS

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Introduction. Diabetes mellitus is a metabolic disease that can affect all the organs, including the liver. The aim of this study was to assess: antioxidant, hepatoprotective and antihyperglycemic effects of *Spirulina maxima* (Sm) in diabetic rats induced by streptozotocin (STZ). **Material and methods.** All solvents and reagents used in this study were reagent grade. Sm powder was purchased from Essential Food for Humanity, Mexico. The method, briefly, was: Twenty-four male rats weighing 150-200 g were divided into four groups of 6 rats each: control (C), control fed with 5% Sm (Sm), STZ-induced diabetes (STZ), and diabetic rats fed on 5% Sm (STZ + Sm). The dose was 60 mg/kg STZ in citrate buffer 0.01 M, i.p., single dose. Non-diabetic animals received the same amount of vehicle. Induction of diabetes was observed at 5 days after the determination of glucose using test strips. The animals were kept and fed for a period of 14 days after STZ administration. At the end of this period were sacrificed by decapitation. Blood was collected and the liver excised. Blood was analyzed for glucose concentration, and liver was analyzed for concentration of TBARS, protein content, as well as the activities of superoxide dismutase (SOD) and catalase (CAT). Data were analyzed with GraphPad prism5, ANOVA. **Results.** Sm feeding significantly reduces glucose levels, cholesterol and triacylglycerols in plasma of rats treated with STZ. With respect to indicators of oxidative stress, Sm feeding increased the plasma activities of SOD and CAT, and reduced the concentration of TBARS in the STZ+Sm group compared to STZ group. There were no significant differences in the concentration of total lipids, TBARS and activities of SOD and CAT in liver. **Conclusions.** The Sm consumption in the diet may be beneficial for controlling the concentrations of glucose, cholesterol and triacylglycerols in diabetic animals, as well as for reduce the oxidative stress. There were no alterations in the liver due to experimental diabetes, probably because the length of the experiment.

TIBOLONE IMPROVES THE LIVER REDOX STATUS OF OVARARIECTOMIZED, HYPERTENSIVE WISTAR RATS

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Purpose. In this work, the effects of tibolone on blood pressure and liver redox status were evaluated in an animal model of estrogen deficiency associated with renovascular hypertension (two-kidneys, one clip, 2K1C). **Material and methods.** Three weeks after the surgical procedures, ovariectomized hypertensive (OVX + 2K1C) Wistar rats were treated with daily doses of tibolone (OVX + 2K1CT rats) or vehicle (OVX + 2K1C), over a period of 15 days. Thereafter, the rats were anaesthetized for direct blood pressure measurements and the evaluation of liver redox status. **Results.** OVX + 2K1C rats presented mean blood pressure significantly higher (+28%), as

compared to control and OVX rats. In OVX + 2K1CT these values became similar to those found in control and OVX rats. Besides, the liver contents of reduced glutathione were increased and of thiobarbituric acid reactive substances (TBARS) contents were decreased in OVX + 2K1CT rats as compared with all other groups. The mitochondrial reactive oxygen species generation, which were increased in OVX + 2K1C rats (+52%), decreased in OVX + 2K1CT rats to values similar to those found in control and OVX rats. Among the antioxidant enzymes studied, stand out the beneficial effect of tibolone on the glucose-6-phosphate dehydrogenase activity, which was significantly reduced in OVX and OVX + 2K1C rats, and was reestablished in OVX + 2K1CT to values similar to control rats. **Conclusion.** Tibolone was effective in reducing the mean blood pressure in OVX + 2K1CT rats and this effect was accompanied of beneficial effects on liver redox status.

GENOTOXIC EVALUATION OF SIMVASTATIN IN MICE WITH NONALCOHOLIC STEATOHEPATITIS

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Objectives. Nonalcoholic steatohepatitis (NASH) is characterized by the association of steatosis with others hepatocellular lesions, essentially balonization and necro-inflammation. The aim is evaluate the genotoxic action of different doses of simvastatin (S) in mice with NASH. **Material and methods.** NASH was induced in C57BL/6 male mice with 8 weeks, through a choline and methionine deficient diet for 4 weeks. The animals were randomly divided into 6 experimental groups: CO+V (control + vehicle carboxymethylcellulose), CO + S4 (S 4 mg/kg), CO + S7 (S 7 mg/kg), CO + S10 (S 10 mg/kg), NASH + V, NASH + S4, NASH + S7, NASH + S10. A 200 μL dose of Simvastatin was administered intragastrically for 2 weeks. The liver tissue was removed to assess DNA damage by comet assay. Data were presented as mean ± standard deviation and statistical analysis by ANOVA followed by Dunnett's test with significance at 5%. **Results.** There was significant increase ($p < 0.01$) in damage index to liver hepatic DNA in groups CO + S7 and CO + S10 compared to CO + V, indicating genotoxic effect of simvastatin in this tissue. The NASH group showed a significantly higher damage index ($p < 0.05$) relative to CO + V, as well as the NASH group who received simvastatin in higher doses ($p < 0.01$). **Conclusion.** The Simvastatin showed a genotoxic effect and has not been able to diminish DNA damage in liver tissues of animals with NASH using 7 and 10 mg/kg.

METHYLPREDNISOLONE AND TRIIODOTHYRONINE PRETREATMENT POST PARTIAL HEPATECTOMY: EFFECT ON DAMAGES, REGENERATION AND LIVER TISSUE RECOVERY

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Purpose. Methylprednisolone and triiodothyronine (MP + T3) pretreatment is one of the strategies developed to increase the viability and functionality of transplanted organs (heart and lungs) from brain-dead donors but the effect on liver is unknown. **Material and methods.** Sprague-Dawley rats were subjected to partial hepatectomy (PHx) of 70% after treatment with MP (0.34 mg/kg), T3 (0.05 mg/kg) or their vehicles in single intraperitoneal injection 3 and 2 hours prior to PHx, respectively. The experimental groups (a. MP + T3, b. vMP + NaOH, c. MP, d. vMP, e. T3 and f. NaOH) were evaluated at 0, 24, 72 and 120 h post resection. The effect of this drugs on the regeneration (mitotic index, Ki67-positive cells), recovery of liver mass (weight of liver remnant), and damage parameters (serum transaminases GOT/ GPT, carbonyl proteins and histology) were analyzed. **Results.** The recovery curve of liver mass did not show significant differences between control (NaOH) and pretreated (MP+T3) animals at any time, however it was observed a significant increase in mitotic index (85%) and Ki-67 positive cells (76.3%) in MP+T3 group compared with controls at 24 hours after HPx. In addition, there was a significant decrease (27%) in the activity of serum transaminases and in levels of carbonyl proteins (71%) ($n = 3$-4, $p < 0.05$, one way ANOVA) in the same groups. Histological analysis confirmed decreased inflammation in pretreated groups compared with controls at 24 h after HPx. **Conclusion.** MP+T3 pretreatment minimizes the inflammatory damage caused by organ resection without showing adverse effects in liver tissue regeneration post HPx.

N-ACETYLCISTEINE REDUCES GASTRIC DAMAGE IN ANIMALS SUBMITTED TO AN EXPERIMENTAL MODEL OF PORTAL HYPERTENSION

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Purpose. To evaluate the effects of N-acetylcysteine (NAC) in animals submitted to an experimental model of partial portal vein ligation (PPVL). **Material and methods.** 24 male Wistar rats divided into 4 groups: 1. sham-operated (SO), 2. PPVL, 3. SO + NAC, administrated from the 8th day after surgery intraperitoneally (10 mg/kg), 4. PPVL + NAC. On the 15th day portal pressure in the mesenteric vein was measured. We evaluated the serum levels of liver function enzymes (AST, ALT and FA) levels of substances reacting to thiobarbituric acid (TBARS), the antioxidant enzymes superoxide dismutase (SOD) and Glutathione peroxidase (GPx), and metabolites of nitric oxide (nitrates and nitrites) in stomach. The histological slides were stained with hematoxylin-eosin. The statistical analysis used was ANOVA followed by Student Newman Keuls test. **Results.** There was no difference between the values of hepatic enzymes. The portal hypertensive group showed an increase in portal pressure, levels of TBARS and nitrates and nitrites when compared to SO group. These values were accompanied by a decrease in superoxide dismutase (SOD) and glutathione peroxidase (GPx) antioxidant enzyme activity. Histology showed dilated vessels in the gastric mucosa in the PPVL group. Treatment with NAC was able to decrease portal pressure values, TBARS and also nitrates and nitrites levels when compared to PPVL group. Furthermore, PPVL+NAC group presented an increase in SOD and GPx activity. In histological evaluation, N-acetylcysteine attenuated damage in gastric mucosa. **Conclusions.** This study suggests that administration of NAC reduces gastric damage in animals with portal hypertension.

EFFECT OF *SPIRULINA MAXIMA* IN AN EXPERIMENTAL MODEL OF HEPATOCELLULAR CARCINOMA

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Purpose. Liver and biliary tract diseases are in sixth place causes of death in adults, in Mexico, so priority alternatives are aimed at prevention. The aim of this study was to assess the antioxidant effects of *Spirulina maxima* (SP) on the development of hepatocellular carcinoma induced by diethylnitrosamine (DENA) and carbon tetrachloride (CCl_4) in an experimental model in the rat. **Material and methods.** 64 male Wistar rats were allocated into 8 groups: control (I), 5%SP diet (II), DENA 200 mg/kg (III), CCl_4 2 mL/kg (IV), DENA + CCl_4 (V), DENA + SP (VI), CCl_4 + SP (VII), DENA + CCl_4 + SP (VIII). DENA and CCl_4 were administered at weeks 0 and 2 (single dose, i.p.); groups II, VI, VII and VIII were fed on 5% SP diet throughout the experiment. After 12 weeks, the rats were killed, plasma was obtained for the assessment of liver function test, the liver was dissected and homogenized for determining the activities of catalase, SOD, GR, GPx, xanthine oxidase, total glutathione, NO, protein carbonyls and TBARS; a fraction of liver was used for histopathology. The results were analysed by ANOVA and Bonferroni test. **Results.** The groups fed on SP diet showed a higher antioxidant activity in liver tissue than in groups fed on control diet. The antioxidant enzyme activities and GSH content were higher in groups fed on SP diet than in the control groups ($p < 0.05$). **Conclusion.** Dietary SP has a protective effect against development of hepatocellular carcinoma, through modification of antioxidant status, this was not showed in liver function test, but it was confirmed by the biochemical studies on liver tissue and by the histopathology analysis.

THE EFFECTS OF ESTROGEN DEFICIENCY ON THE LIVER REDOX STATUS OF OVARIECTOMIZED MICE

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Purpose. The aim of this work was to evaluate the liver redox status in an animal model of estrogen deficiency associated with hepatic steatosis. **Material and methods.** Ten weeks after the surgical procedures of ovary removal, ovariectomized (OVX) Swiss mice were anaesthetized for the liver removal and measurements of lipid contents, mitochondrial and peroxisomal reactive oxygen species (ROS) generation and determinations of the activities of antioxidants enzymes. The existence of oxidative damage in the liver was assessed by the detection of the thiobarbituric acid reactive substances (TBARS). The results were compared with those obtained with control (sham-operated) mice. **Results.** OVX mice presented significantly higher amounts of total liver lipid contents (+30%) and this was associated with higher mitochondrial ROS generation. The peroxisomal β-oxidation, which contributes with approximately 35% of all oxygen peroxide produced in the cell, was increased in OVX mice. However, the activity of catalase was reduced in 41.6% in these animals. Besides, the activities of the other antioxidant enzymes, namely, glutathione peroxidase, glutathione reductase and glucose 6-phosphate dehydrogenase were all reduced in OVX mice. These matched effects could lead to oxidative damage, a condition that was, in fact, evidenced by the elevated levels of TBARS found in livers of OVX mice. **Conclusions.** The fat liver accumulation was accompanied by higher mitochondrial and peroxisomal ROS generations in OVX mice and these, associated with a reduction in the cellular enzymatic antioxidant defenses, resulted in oxidative damage of livers from OVX mice.

HEPATOPROTECTIVE EFFECT OF THE COFFEE ON THIOACETAMIDE-INDUCED LIVER DAMAGE IN RATS

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Purpose. Previous clinical observations suggested that coffee might have beneficial effects on the liver. However, the action mechanism of coffee has not been established. This study was to evaluate the antifibrotic properties of coffee in a model of liver damage induced by repeated administration to thioacetamide (TAA) in male Wistar rats. **Material and methods.** In this work, cirrhosis was induced by chronic TAA administration and conventional coffee or decaffeinated coffee (CC, DC, respectively) co-administered for 8 weeks. **Results.** TAA administration elevated serum alkaline phosphatase, γ-glutamyl transpeptidase and alanine aminotranspherase, liver lipid peroxidation, collagen content, depleted liver glycogen and glutathione peroxidase (GPx) activity. Additionally there were increased levels of proteins: TGF-β, CTGF and α-SMA, MMP-2, 9 and 13. Coffee prevented most of the changes produced by TAA. Histopathological analysis was in agreement with biochemical and molecular findings. The best effect was produced by CC. **Conclusions.** Our results indicate that coffee prevents experimental cirrhosis; the action mechanisms are probably associated to its antioxidant properties and mainly by its ability of blocking the elevation of the profibrogenic cytokine TGF-β and CTGF. Various components of coffee that have been related to such a favorable effect including caffeine, coffee oils kahweol, cafestol, and antioxidant substances, but no definite evidence is available for any of these components. These findings suggest a beneficial effect of coffee on the liver. However, more basic and clinical studies must be performed before reaching a final recommendation.

THE EFFECT OF DIETHYLNITROSAMINE IN LIVER FUNCTION TESTS AND HISTOLOGY OF RATS LIVER

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Objectives. Was to evaluate the effect of hepatotoxic agent diethylnitrosamine (DEN) as a model to study liver injury, measuring the liver function tests (LFTs) and determining the histological. **Material and methods.** 20 male Wistar rats, ± 270 g were divided into four groups: (I) Control (7 weeks), (II) DEN7 (III) CO10 (10 weeks), (IV) DEN10. Groups II and IV received DEN twice a week 50 mg/kg ip for 7 and 10 weeks. In the 7th and 10th weeks, blood was collected for LFTs: transaminases (AST and ALT), gamma glutamyl transferase (GGT) and alkaline phosphatase (ALP) (U/L). Liver samples were removed for histological analysis. The statistic analyze used was the Student t test with $p < 0.05$. **Results.** The LFTs show differences between groups. The values were: AST (I) 116.7 ± 25.7 (II) 1241.4 ± 683.5 (III) 99.5 ± 16.4 (IV) 94.7 ± 224.0; ALT (I) 49 ± 9.5 (II) 428.1 ± 218.9 (III) 50 ± 6.0 (IV) 32.5 ± 104.0; GGT (I) 0.75 ± 0.9 (II) 8.7 ± 4.4 (III) 0.75 ± 0.9 (VI) 5.0 ± 2.8 ALP (I) 124.2 ± 38.8 (II) 188.6 ± 57.3 (III) 136.0 ± 29.9 (IV) 442.5 ± 103.9; the group II shows significant increase compared to group I $p < 0.05$. The liver histology with DEN at 7 weeks showed changes in hepatic architecture with intense ductal proliferation. Hepatocytes with enlarged

nuclei, extremely atypical, steatosis and extensive loss of parenchyma. At week 10, changes are still remain, being possible to verify cholestasis, cholangitis, necrosis and more diffuse nuclear atypia. **Conclusion.** The use of DEN caused intense inflammatory process and deterioration in liver. Based on the evaluated data we show signs of cholangitis by the histological appearance and the values of ALP and GGT, signaling cholestatic disease.

DECREASE OF GENE EXPRESSION OF TGF-β IN HUH CELLS USING AN ADENO-ASSOCIATED VECTOR EXPRESSING A TRUNCATED RECEPTOR TYPE II FOR TGF-β

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Purpose. Generate an AAV2/8-TβRIIΔcyt and evaluate its effect on gene expression of TGF-β, Col-I and MMP-2 in culture. **Material and methods.** Vector was generated subcloning the TβRIIΔcyt cDNA into the HindIII/XhoI site of pAAV-MCS. TβRIIΔcyt insertion was confirmed by restriction map and sequencing. Cotransfection of pHelper, p5E18 and PMCS-TβRIIΔcyt or PITR-GFP was performed in HEK-293 cells with polyethyleneimines at a concentration of 15, 10 and 10 μg of plasmid respectively. 48 h post-transfection, cells were lysed and viral particles were purified by iodixanol gradient and quantified by qPCR. For *in vitro* assays, $2x10^6$ Huh 7.0 cells were seeded and divided into 4 groups: Control, rTGF-β, rTGF-β+AAV-GFP (irrelevant gene) and rTGF-β+AAV-TβRIIΔcyt (therapeutic gene). 48 h post-transduction (1×10^{11} cg/mL), conventional PCR was performed for transgene detection and qPCR to assess gene expression of TGF-β, Col-I and MMP-2. For statistical analysis ANOVA and Bonferroni post-hoc test was performed. **Results.** We obtained 1×10^{12} cg/mL of AAV2/8-GFP and 1×10^9 cg/mL of AAV2/8-TβRIIΔDcyt. In Huh 7.0 cell culture TβRIIΔcyt delivered into an adeno-associated virus was expressed efficiently. Treated cells with VAA2/8-TβRIIΔcyt showed a significant decrease in gene expression of TGF-β ($p < 0.05$) and a tendency to decrease in Col-I and MMP-2 gene expression, without statistical differences in these genes. **Conclusions.** We generated adeno-associated virus containing a truncated type II receptor for TGF-β1. Gene expression of TβRIIΔcyt was able to decrease gene expression of this cytokine *in vitro* in a human hepatocyte cell line. We conclude that gene therapy using VAA2/8-TβRIIΔcyt can be useful for treatment of liver fibrosis.

QUERCETIN DECREASES HEPATIC FIBROSIS BY REDUCING HEPATIC STELLATE CELLS AND REGULATING THE BALANCE OF PRO AND ANTI-FIBROGENIC MOLECULES

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Introduction. In the past we have showed that quercetin prevents liver damage by decreasing oxidative stress and inflammation. However, quercetin effect on the molecular mechanisms of hepatic fibrosis degradation, HSC activation and apoptosis has not been elucidated. **Purpose.** To elucidate the effect of quercetin on the activation and apoptosis of HSC and on molecular mechanisms in an experimental model of cirrhosis. **Material and methods.** Wistar male rats were chronically intoxicated with CCl4 for eight weeks and concomitantly treated with quercetin (150 mg/kg/day). Animals were sacrificed, liver samples were taken for histology (Masson stain, sirious red, immunohistochemistry and TUNEL assay), gene expression of profibrogenic genes (Col-1 TGF-β1 and CTGF), anti-fibrogenic genes (TGF-β3), metalloproteinases (MMP2 and MMP9). Activity of MMPs was analyzed by zimography and NFkb activity by gel-shift. **Results.** Animals concomitantly treated with quercetin presented significantly less expression of profibrogenic genes. Cirrhotic animals presented a fibrosis and collagen index of 22.5% and 35% while rats treated with quercetin showed a fibrosis and collagen index of 10.76% and 10.52% respectively. NF-κb activity decreased significantly with the treatment. Antifibrogenic gene TGF-β3 increased the expression with quercetin. Apoptosis of HSC was determinate by TUNEL assay and activation determinated by positive cells to α-sma by immunohistochemistry, showed number of apoptotic cells increased 17.8 times and the activation decrease 55% in animals treated with quercetin. Activity of MMP2 increased three times while MMP9 two times with quercetin treatment. **Conclusions.** Quercetin inhibits HSC activation, promotes their apoptosis and stimulates activity of MMPs which is reflected on stage of fibrosis.

PROTECTIVE EFFECT OF BIXIN AGAINST THE HEPATOTOXICITY INDUCED BY CARBON TETRACHLORIDE IN RATS

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The liver has a great importance in the animal body since it is responsible to the biotransformation of exogenous chemicals (xenobiotics), making the liver tissue a potential target for toxic substances. The carotenoid bixin from annatto seeds *(Bixa orellana L.)* is an antioxidant that can contribute to protecting cells and tissues against the deleterious effects of free radicals. In the present study we evaluated the protective effect of the bixin on liver damage caused by carbon tetrachloride (CCl_4) in rats. Male Wistar rats weighing approximately 200-240 g were used. The animals received food and water *ad libitum* and were divided in four groups of six animals according each treatment: group 1 (control) received canola oil by gastric gavage for 7 days and mineral oil (0.5 mL/kg body weight, intraperitoneally) in the last day of treatment; group 2 received the bixin, dissolved in canola oil, by gastric gavage (5 mg/kg body weight) for 7 days and mineral oil on the last day of treatment; group 3 received canola oil by gastric gavage for a period of 7 days and a single dose of CCl_4 diluted in mineral oil (0.125 mL/kg body weight, intraperitoneally) in the last day of treatment; group 4, received the bixin by gastric gavage (5 mg/kg body weight) for 7 days and a single dose of CCl_4 diluted in mineral oil (0.125 mL/kg body weight, intraperitoneally) in the last day of treatment. After euthanasia, the blood of treated and control animals was collected and the serum activities of alanine aminotransferase (ALT) and aspartate aminotransferase (AST) were analyzed. The livers were removed and after preparation of the homogenate the activity of the enzyme glutathione reductase (GR), the levels of reduced glutathione (GSH) and NADPH, as well as the peroxidation of membrane lipids were determined. Bixin protected the liver damage caused by CCl_4 as noted by the significant decrease of the release of the enzymes ALT and AST. Bixin also protected the liver against the oxidizing effects of CCl_4, since it preven-

ted the decrease in GR activity and levels of GSH and NADPH. The peroxidation of membrane lipids was also inhibited by bixin. Therefore, we can conclude that the protective effect of bixin against hepatotoxicity caused by CCl_4 is related to the antioxidant activity of the compound.

EVALUATION OF IMMP AS ANTI-FIBROTIC ON EXPERIMENTAL LIVER

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Purpose. The aim of this study was to evaluate the anti-fibrotic effect of Immunomodulatory metalopeptide (IMMP), in a liver fibrosis model immunologically induced. **Material and methods.** 32 male Wistar rats (150 g) were divided into 4 groups (n = 8): 1. Control: PBS 0.5 mL i.p. 3-times per week for 8-weeks; 2. IMMP: 50 ng/kg i.p. 3-times per week during 4-weeks; 3. Fibrosis: porcine serum 0.383 mg/kg i.p. twice per week for 8-weeks; 4. Fibrosis+IMMP: doses mentioned above; IMMP treatment started at the fifth week. Rats were sacrificed using CO_2 chamber, serum level of IL-6 was analyzed by ELISA. Collagen content of the liver was determinate by hydroxyproline assay, three-micron-thick sections were stained with Masson for analysis of collagen, also used for immunohistochemistry of TGF-b1. **Results.** Fibrosis group had an increase in IL-6 (2.6-fold), alterations in parenquima and fibrosis extending around central veins and portal structure, an increase in collagen content (4.6-fold) and had a huge expression of TGF-b1 in hepatocytes around collagen fibers, all compared with control ($p < 0.05$). Rats with fibrosis treated with IMMP had a reduction of IL-6 (24.6%), showed a reduction in parenquima alterations and less fibrosis around central veins and portal structures, we observed a reduction in collagen content (63.14%) and reduced expression of TGF-b1 on rats with fibrosis, which were seen as small dispersed zones of hepatocytes around parenquima, all compared with fibrosis ($p < 0.05$). **Conclusions.** The treatment of IMMP reduced liver fibrosis by reduction of inflammatory and activator mediators, resulting in a decrease of fibrosis development.

EL FACTOR DE CRECIMIENTO DE HEPATOCITOS PROTEGE CONTRA EL EFECTO HEPATOTÓXICO INDUCIDO POR LA RIFAMPICINA Y LA ISONIAZIDA

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Introducción. La tuberculosis es una enfermedad con alto impacto a nivel hepático debido al incremento en la resistencia a los antibióticos de *M. tuberculosis,* lo cual conduce al incremento de dosis o tiempo de tratamiento con antibióticos usados convencionalmente, como la isoniazida y la rifampicina, que suelen ser administrados a diario o intermitentemente por varios meses, incrementando la posibilidad de daño hepático. La biotransformación de los fármacos genera especies reactivas de oxígeno (ROS) que inducen daño hepatocelular. El factor de crecimiento de hepatocitos (HGF) demostró el incremento de las defensas antioxidantes en los hepatocitos. **Objetivo.** Estudiar el papel protector del HGF en la hepatotoxicidad inducida por rifampicina (RMP) e isoniazida (INH) en ratones de la cepa CD1. **Material y métodos.** Los ratones fueron separados en cuatro grupos: el grupo control (A) sólo recibió solución salina isotónica intragástrica, el grupo B recibió RMP 150 mg/kg + INH 75 mg/kg intragástrica, el grupo C recibió 10 mg/kg de HGF + RMP y INH, el grupo D sólo recibió HGF. Adicionalmente un grupo E recibió anti-HGF 5 ng/kg + RMP y INH para corroborar los efectos del HGF endógeno. Se realizaron tinciones rutinarias de H&E, se determinó por microscopia confocal apoptosis por TUNEL y caspasa 3, ROS por dihidroetidio (DHE) y diclorofluoresceína (DCFH), así como pruebas de función hepática como AST. **Resultados.** Los fármacos indujeron muerte celular por apoptosis y esteatosis juzgado por las histologías de H&E, la apoptosis se corroboró por microscopia confocal con TUNEL y caspasa 3 activa y se encontró un incremento significativo de AST. Se determinó un incremento de ROS, particularmente peróxidos por DCFH y anión superóxido por DHE. Todos los marcadores de daño se llevaron a valores control con el tratamiento de HGF. El grupo control E mostró exacerbación de los efectos tóxicos de los fármacos, demostrando que aún el HGF endógeno confiere cierta protección hepática. **Conclusión.** El HGF ejerció un efecto protector, controlando el estrés oxidante y evitando el daño hepatocelular. CONACyT # 131707.

EVALUACIÓN DEL EFECTO HEPATOTÓXICO Y HEPATOPROTECTOR DE SUPLEMENTOS DIETÉTICOS Y/O FITOFÁRMACOS A TRAVÉS DE UN MODELO *IN VITRO* EN CORTES PRECISOS DE REBANADAS DE HÍGADO DE RATAS

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Introducción. Según la OMS 80% de la población utiliza medicina alternativa y complementaria (MAC); se ha descrito que 30 a 80% de los pacientes de clínicas de hígado utilizan remedios herbarios. **Objetivo.** Evaluar la actividad hepatotóxica y hepatoprotectora de tres suplementos dietéticos y/o fitofármacos más utilizados para el tratamiento de enfermedades hepáticas a través del modelo *in vitro* de cortes precisos de rebanadas de hígado de rata. **Material y métodos.** Los compuestos analizados fueron: Áloe vera, Cardo lechoso y Boldo. Las presentaciones de los compuestos fueron: Áloe vera: Omnilife, Herbalife y GNC; Cardo lechoso: GNC, Liver Med (Medix); Legalon (Nycomed), Boldo: té (Therbal), cápsula (Botnatura) y pastilla (Anahuac). Las rebanadas de hígado de ratas Wistar se obtuvieron con un rebanador Brendel Vriton. Los grupos de estudio fueron (n = 5): control (rebanadas sin tratamiento), control de toxicidad (rebanadas tratadas con acetoaminofen 15 mM), y los grupos de estudio que fueron rebanadas tratadas con cada uno de los tres productos referidos más acetoaminofen 15 mM. Se incubaron las rebanadas por 36 h y posteriormente se realizó análisis enzimático e histológico. **Resultados.** La toxicidad en los niveles de ALT y AST fueron: 1) Áloe vera (ALT): Control < GNC < Omnilife < Herbalife; (AST): GNC < Control < Herbalife < Omnilife. 2) Boldo (ALT y AST): Control < té < Cápsula < pastilla. 3) Cardo lechoso (ALT y AST): Control < Liver Med < Legalon < GNC. Los productos para evaluar hepatoprotección fueron Áloe vera (GNC), Boldo (té de Therbal) y Cardo lechoso (Legalon de Nycomed). Este último se eligió por ser un extracto estandarizado y muy usado por hepatópatas y no en relación con los resultados de los parámetros enzimáticos evaluados.

Se encontró que el Áloe vera (GNC) en AST y el Legalon (Nycomed) en ALT y AST fueron los productos hepatoprotectores (Figuras 1 y 2).

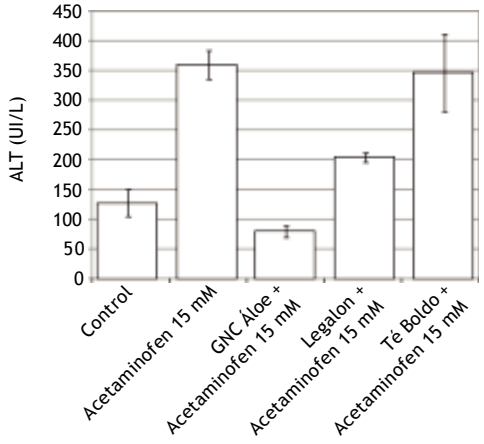

Figura 1. ALT (UI/L) a las 36 horas.

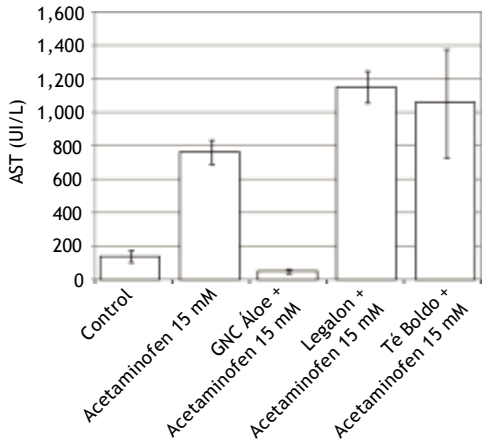

Figura 2. AST (UI/L) a las 36 horas.

A nivel histológico los hallazgos fueron: Grupo de toxicidad: dilatación sinusoidal y centrilobulillar, predominio de focos de esteatosis y, focalmente, necrosis hepatocelular. Áloe vera (GNC): estructura más conservada, congestión sinusoidal, escasos focos microscópicos de necrosis. Legalon: estructura conservada, escasos focos de esteatosis y de daño hepatocelular. Boldo (té): múltiples focos de esteatosis y signos de necrosis perivenular. **Conclusiones.** El Áloe vera, el Cardo lechoso y Boldo son de los productos naturistas más utilizados por los pacientes hepatópatas. Los productos menos tóxicos fueron Áloe vera de GNC, Boldo té de Therbal y Legalon. Los productos hepatoprotectores fueron Áloe vera de GNC y Legalon de Nycomed. El modelo experimental mostró ser útil para valorar la toxicidad y/o hepatoprotección de productos naturistas.

HEPATOTOXICIDAD Y PATRONES MORFOLÓGICOS

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Objetivo. Determinar los patrones histopatológicos de toxicidad hepática por drogas. **Material y métodos.** Se revisaron archivos de Patología de cinco años (2007-2011), con el antecedente de usar alguna medicación y con daño hepático, ya fuera agudo o crónico. Se reevaluaron las secciones histológicas para determinar algún patrón morfológico que explicara la clínica del paciente. **Resultados.** Se encontraron cinco pacientes con daño hepático: Dos casos de ductopenia asociada al ácido clavulínico y ciproterona; un caso de hepatitis aguda asociado a isoniacida; un caso de fibrosis hepática asociada a metothrexate**. Conclusión.** El patrón morfológico relacionado con mayor frecuencia con la injuria por drogas es la ductopenia. La toxicidad por drogas debe considerarse como parte del diagnóstico diferencial ante el hallazgo histológico de ductopenia.

PARTICIPAÇÃO DO ESTROGÊNIO NA PREVENÇÃO DO ESTRESSE OXIDATIVO NO MODELO DE LIGADURA PARCIAL DA VEIA PORTA EM RATAS WISTAR

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Objetivo. A ligadura parcial de veia porta (LPVP) é o modelo experimental utilizado em ratos para estudar os mecanismos fisiopatológicos envolvidos na hipertensão portal pré-hepática. A Hipertensão Portal (HP) é uma complicação secundária à cirrose que causa o surgimento de circulação colateral hiperdinâmica. O estrogênio é uma molécula antioxidante com diferentes ações fisiológicas. Assim, o objetivo deste trabalho foi verificar a ação antioxidante do estrogênio endógeno em modelo experimental de LPVP comparando ratas intactas com ratas castradas. **Métodos.** Foram utilizadas 20 ratas Wistar, pesando 250g, divididas em 4 grupos: sham-operated (SO); intactas com ligadura parcial da veia porta (IL); castradas (C) e castradas com ligadura parcial da veia porta (CL). No 1º dia: foi realizada a castração ou sham-operated; no 7º dia a cirurgia de LPVP; no 15° dia após a LPVP, foi verificada a pressão portal (PP) na veia mesentérica das ratas, no polígrafo Letica. A lipoperoxidação no estômago foi avaliada através da técnica das substâncias reativas ao acido tiobarbitúrico (TBARS) e a atividade das enzimas antioxidantes superóxido dismutase (SOD), catalase (CAT) e glutationa peroxidase (GPx). A análise estatística foi ANOVA - Student-Newmann-Keuls, (Média ± EP), foi considerado significativo para $p < 0.05$. **Resultados.** Não foi detectado o estradiol no plasma das ratas castradas. A PP mostrou um aumento significativo no grupo CL em relação aos demais, não houve diferença significativa no grupo das ratas intactas (SO: 14,66± 2,90; IL: 21,21 ± 1,70; C: 22,16 ± 4,92 e CL: 34,36 ± 2,59 – mm/Hg). O TBARS aumentou significativamente no grupo C e CL, em relação às demais (SO: 0,53 ± 0,07; IL: 0,91 ± 0,17; C: 3,60 ± 1,23 e CL: 4,02 ± 1,05 - nmoles/mg Prot). Quanto às enzimas antioxidantes, as ratas castradas e com posterior LPVP, tiveram aumento significativo em relação às demais; para a SOD (SO: 35,59 ± 7,90; IL: 27,18 ± 1,44; C: 80,73 ± 2,5; CL: 112,64 ± 9,8 - U SOD/mg de Prot); para a CAT (SO: 0,14 ± 0,02; IL: 0,12 ± 0,01; C: 0,24 ± 0,005; CL: 0,35 ± 0,06 – pmoles/mg de Prot); para a GPx (SO: 0,67 ± 0,28; IL: 0,51 ± 0,18; C: 4,20 ± 0,06 e CL: 0,57 ± 0,02 - nmoles/mg de Prot). **Conclusão.** Neste modelo experimental de LPVP, as ratas intactas estão mais protegidas que as castradas quando avaliamos o estresse oxidativo. A diferença entre os dois grupos é a castração, onde foi observado ausência do estrogênio circulante. Podemos sugerir que o estrogênio, por apresentar radicais hidrofenólicos em sua molécula, desempenha um papel protetor nas ratas intactas em comparação com as castradas, agindo assim como antioxidante, neste modelo experimental.

A AÇÃO DA ANTIOXIDANTE QUERCETINA MODULANDO OS PARÂMETROS MOLECULARES DO PROCESSO INFLAMATÓRIO EM CAMUNDONGOS COM ESTEATO-HEPATITE NÃO ALCOÓLICA EXPERIMENTAL

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Objetivos. A Esteato-Hepatite Não Alcoólica (EHNA) é uma das mais comuns doenças hepáticas, muitas vezes silenciosa, com alta incidência, diagnóstico difícil e ainda sem terapias eficazes. A característica importante na EHNA é de acúmulo de gordura no fígado, juntamente com a inflamação e progressiva fibrose. Este estudo objetiva desenvolver um modelo experimental de EHNA através de uma dieta deficiente em metionina e colina (MCD) e avaliar as alterações hepáticas, parâmetros de estresse oxidativo, lipoperoxidação e parâmetros moleculares de inflamação, verificando a ação resultante da suplementação do flavonóide antioxidante quercetina (Q). **Métodos.** Utilizou-se camundongos machos C57BL6, divididos em quatro grupos (n = 8): CO + V (ração controle, além de carboximetilcelulose sódica à 1% usada como veículo), CO + Q (50 mg/kg via intragástrica), EHNA + V (dieta MCD) e EHNA + Q. As dietas e a suplementação de Q foram administradas por 4 semanas. Foram avaliados os níveis hepáticos de mRNA de TNF-α, COX-2, HMGB-1 e TGF-β através de *real time* PCR (unidades arbitrárias).O trabalho foi aprovado pelo Comitê de Ética e Pesquisa do HCPA. Os dados são apresentados como média ± erro padrão, tratados por ANOVA seguido de teste *Student Newman Keuls* com significância de 5%. **Resultados.** O grupo EHNA + Q comparado com EHNA + V mostrou um decréscimo significativo na enzimas de integridade hepática dos grupos 4 semanas (AST: 327,92 ± 24,08 *vs.* 469,86 ± 49,16, ALT: 335,94 ± 19,41 *vs.* 687,33 ± 51,54 U/L), bem como na lipoperoxidação (TBARS: 6,90 ± 0,96 *vs.* 8,03 ± 1,53 nmoles/mg prot) e melhoria nos parâmetros moleculares do processo inflamatório através de TNF-α (4,05 ± 0,6 *vs.* 7,65 ± 0.7), COX-2 (3,52 ± 0,2 *vs.* 7,08 ± 0,8), HMGB-1 (0,93 ± 0,2 *vs.* 2,39 ± 0,4) e TGF-β (0,87 ± 0,4 *vs.* 0,61 ± 0,3). O diagnóstico de EHNA foi realizado em 100% dos camundongos que receberam a dieta MCD, mostrando histologicamente menor grau de esteatose macrovesicular, balonização e processo inflamatório no grupo tratado com Q, bem como redução da marcação de células estreladas por imuno-histoquímica (α-SMA: 0,79 ± 0,4 *vs.* 1,48 ± 0,9% de pixels corados). **Conclusão.** Os resultados demonstram que Q 50 mg/kg reduziu os níveis de lipoperoxidação, parâmetros inflamatórios e fibrose no fígado, bem como os níveis das enzimas de integridade hepática, sugerindo efeitos protetores do fígado neste modelo.

INFLAMAÇÃO HEPÁTICA E PULMONAR NA HIPÓXIA INTERMITENTE SIMULANDO A APNÉIA DO SONO

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Apnéia do sono é um distúrbio respiratório que leva ao colapso momentâneo e cíclico das vias aéreas superiores, levando ao quadro de hipóxia intermitente (HI). A HI pode levar a formação de radicais livres que contribui para o estresse oxidativo, sendo possivelmente esse o mecanismo central da relação entre apnéia do sono e esteato hepatite não alcoólica. Objetivamos investigar o mecanismo de inflamação no modelo animal de hipóxia intermitente, simulando a apnéia do sono, tanto no tecido pulmonar quanto no hepático. Utilizamos 12 camundongos, machos, C57BL/6, divididos em dois grupos (SHI - simulação de HI; e HI - que foi exposto a HI por 35 dias) Observamos que houve aumento do dano oxidativo (TBARS - pulmão: SHI 4,57 ± 0,10; HI 5,22 ± 0,10/fígado: SHI 2,90 ± 0,23; HI 3,76 ± 0,15) e alteração nas enzimas antioxidantes endógenas (SOD: pulmão: SHI 7,27 ± 0,99; HI 4,64 ± 0,22/ fígado: SHI 3,13 ± 0,53; HI 5,86 ± 0,70/CAT: pulmão: SHI 2,62 ± 0,18; HI 3,48 ± 0,13/fígado: SHI 0,82 ± 0,17; HI 2,33 ± 0,09) nos camundongos expostos à HI. Valores elevados de expressão, no grupo HI, dos fatores de transcrição: hipóxia induzível (HIF-1a - pulmão: SHI: 0,26 ± 0,05; HI: 0,51 ± 0,04/fígado: SHI: 0,57 ± 0,02; HI: 0,68 ± 0,02), nuclear (NF-kb - pulmão: SHI: 0,10 ± 0,006; HI: 0,13 ± 0,016/fígado: SHI:0,07 ± 0,007; HI: 0,17 ± 0,06) e necrose tumoral (TNF-a - pulmão: SHI: 0,96 ± 0,08; HI: 1,33 ± 0,08/fígado: SHI: 0,47 ± 0,09; HI: 0,70 ± 0,03), bem como elevação da expressão da NO sintase induzível (iNOS - pulmão: SHI: 0,72 ± 0,10; HI: 0,97 ± 0,16/fígado: SHI: 0,52 ± 0,12; HI: 0,94 ± 0,03), fator de crescimento vascular endotelial (VEGF – pulmão: SHI: 1,00 ± 0,08; HI 1,23 ± 0,03/fígado: SHI: 0,21 ± 0,04; HI: 0,36 ± 0,01) e Caspase 3 clivada (pulmão: SHI: 0,08 ± 0,01; HI: 0,28 ± 0,04/ fígado: SHI: 0,29 ± 0,07; HI: 0,83 ± 0,07). Demonstrando que a exposição à hipóxia intermitente por 35 dias, simulando a apnéia do sono, leva ao estresse oxidativo, inflamação e apoptose no fígado e pulmão.

MISCELLANEOUS

HEPATOTOXICITY BY HERBS. SEVERE CHOLESTASIS BY RICA-RICA. CLINICAL CASE

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Aim. To present a case of acute cholestasis secondary to the ingestion of the grass "Rica-Rica" with chronic evolution and liver fibrosis. This herb, *Acantholippia salsoloides*, originate from Bolivian plateau is used with infusions of yerba mate or tea for dyspepsia. **Case.** Female patient, 26 years with a history of 45 days of itching, jaundice, and fever, aspartate transaminase x 5 times normal value (nv), alanino transaminase x 10 nv, bilirubin 20 mg/dL (70% conjugate) alkaline phosphatase x 7 nv, Gamaglutamiltranspeptidase x 20 nv, cholesterol 631 mg%, hemoglobin 9,2 gdL, white blood cells 11,000 m^3. Autoimmune and viral markers were negative, ultrasound and a MR cholangiography without signs os dilatation of the bile ducts. A liver biopsy (BX) showed: diffuse duct proliferation, cholangitis and pericholangitis; severe cholestasis hepatocanalicular, centrilobular and in midzone. Acute cholestatic hepatitis with eosinophils compatible with hepatotoxicity. She started treatment with UDCA (12 mg/kg/d) and 20 mg/d of methylprednisolone. Further questioning brought the use of "Rica-Rica" consumption, 5 g/twice/day, with yerba mate for 15 days. At the third month itching and biochemistry cholestasis persists. A BX showed moderate cholestasis hepatocanalicular and marked peripheral duct proliferation. Fibrosis F2. Another BX at 2 years of evolution reveals persistence of cholestasis and hepatic fibrosis F3. **Conclusions.** In cases of drugs hepatotoxicity the lesion may persist even suspending the poison, the duration and severity is unpredictable and sometimes dose independent. This would be the first reported case of hepatotoxicity by Rica-rica, an herb over the extensive list of herbs causing liver injury.

ASYMPTOMATIC HEPATIC HYDATIDOSIS. A CONTRIBUTION TO THE OPTION TO WATCH AND WAIT

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Introduction. The liver is the organ most frequently affected by the echinococcus granulosus (EG) acquired mostly in childhood. The use of ultrasound (US) showed an unexpected high prevalence of the disease mostly asymptomatic, raising questions about whether to treat or not this asymptomatic carriers. The objective was to analyze the years lived outside endemic areas in liver cyst carriers who were attended between 1998-2010 as a contribution to the knowledge of the natural history of the disease. **Material and methods.** The records from patients with liver hydatid disease were revised. The diagnosis was based on the US images according to the WHO US classification. Age, geographic area where they came from, types of cyst, symptoms and the time elapsed since they leave the endemic area were analyzed. **Results.** 55 patients, mean age 52 years (19 to 86) were seen. In 49 the time they lived outside the endemic area were assessed: the average was 21 years (3 to 67). All but 2 continued to be asymptomatic. Three patients continued to live in the rural area and 4 symptomatic patients underwent surgery. **Discussion.** The great tolerance of the liver for EG infestation raised questions about the need to treat or not to treat this asymptomatic liver carriers. This work is another contribution to the watch & wait option based on the long time (3 to 67years) without symptoms.

LIVER ELASTOGRAPHY: RESULTS AFTER TWO YEARS IN A CENTER OF HEPATOLOGY IN ARGENTINA

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Background. The transicional elastography (FibroScan®) is an approved noninvasive tool for the evaluation of the fibrosis in patients with chronic hepatopathy. **Objective.** To present the characteristics of the studies made until November of 2011. **Material and methods.** All variables were collected in case of being available. Studies were made by three experienced operators and a medium probe was used. The study with a success rate > 60% and IQR < 30% was considered valid. **Results.** 1976 studies were made. The duration average of the study was of 8.9 min. Complications were not registered. The requests were made by doctors of the hospital (42,6%) and externals (57,4%), being the cause of hepatopathy HCV in 46,3% of the studies, NASH 21,3%, HBV 19,7%, others 12,7%. Valid results in 7,9% of the patients could not be obtained, the 97,2% of these patients had a BMI > 28; of any way there were 226 patients with BMI > 28 in that the study was made without difficulties. All the patients with cirrhosis by ecography (n: 93) had fibroscan compatible with F4 of METAVIR. In 453 (22,9%) patient we could obtain a liver biopsy (≥ 7 portal spaces) simultaneous with fibroscan (difference < 6 months). We observed an agreement of 83% in global form, 95% of the discordancy was of a single stage. **Conclusion.** The elastography is present in the study of chronic hepatitis. The maintained demand of the method after two years of use we thought that it is correlated with its acceptance.

PROSPECTIVE FOLLOW UP WITH FIBROSCAN AND LIVER BIOPSY IN PATIENTS WITH HEPATITIS C

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Introduction. The evaluation of the liver fibrosis is relevant to the prognosis and the possible determination of treatment in the patients with chronic hepatitis C. In this background the Fibroscan is accepted and the possibility of making a prospective follow up in these patients is important, fundamentally for those without initial indication of treatment. **Objective.** To present the correlation between liver biopsy and Fibroscan in patients HCV + and their prospective follow up. **Material and methods.** The studies were analyzed from October 2009 to November 2011. **Results.** 914 Fiborscans were made in 690 HCV patients; 86 patients had a correlated liver biopsy (≤ 6 months of difference). The correlation between biopsy and elastography was 84%. One year after both studies, 52 patients had a second control fibroscan (FS1) and 12 patients were controlled with a third fibroscan (FS2). The result of the FS1 was just as the initial in all the patients. Of the 12 patients with FS2: 7 had F0-F1 in control from the beginning. The 5 rest initiated treatment in 2010 due to F ≥ 2 by fibroscan and biopsy. The fibroscan at 3 years remains without significant changes. Of the 86 initial patients, 5 died: all with fibroscan greater to 28 kPa. **Conclusion.** In spite of being a small series, the follow up of liver fibrosis in patients HCV +, it seemed to be feasible with elastography. As the number of patients are increasing, we will be able to compare our series with the studies published.

COMPLEMENTARY AND ALTERNATIVE MEDICINE PREVALENCE AMONG GASTROENTEROLOGY PATIENTS IN CHIAPAS

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Purpouse. To determine the prevalence, the variety most used and reasons for using complementary and alternative medicine (CAM) between service patients Gastroenterology. **Material and methods.** Statistical Analysis, Univariate, measures of central tendency and dispersion. A structured survey was performed by 6 questions related to the use, consumption, range and reasons for using MAC products, from April 1st to 30th 2011 with patients over 15 years of both sexes who came the outpatient gastroenterology morning shift at the General Hospital of Zone 2 of the Instituto Mexicano del Seguro Social in the city of Tuxtla Gutiérrez, Chiapas, Mexico. Parameters were considered age, sex, occupation and origin. Consent was requested, informing the basis of the survey protocol evaluated and approved by Local Research Committee of the hospital, R2011-record 702-1. **Results.** Of 966 surveys 32.71% (n = 316) were male and 67.28% (n = 650) were female, 68.53% (n = 662) and 31.46% yes (n = 304) negative with the consumption of MAC. With a prevalence in our group of 4.2%. Among 662 different reasons were identified affirmative: digestive tract 32.55% (n = 252), not specified 15.11% (117),* obesity 6.5% (n = 51). Energy metabolism and urinary motives 49 cases in each category and a 6.3% share each, neurological 6.07% (n = 47), respiratory 4.5%, 3.2% nutritional supplement (n = 25), gynecological 2.3% (n = 18), cancer 2.19% (n = 17). Immune (n = 15) and haematological (n = 15) 1.9% each, bones and joints 1.42% (n = 11), less than 1% dermal, cardiovascular, collagen diseases and ophthalmology. Digestion of the reasons include: gastritis (n = 72), abdominal pain (n = 51), upset stomach (n = 25), colitis (n = 17), constipation (n = 17), intestine (n = 16) , diarrhea and flatulence (n = 13) each, liver (n = 11), VB (n = 8), reflux (n = 1), hemorrhoids (n = 3), heartburn (n = 1), vomiting (n = 1). The average age was 48.7 years, predominant age group

between 51 and 60 and which corresponds to 21.73% (n = 210) individuals. In relation to the activity: 52.89% (n = 511) housewives, 10% (n = 105) Professional, 9.2% (n = 89) employees, 7.86% (n = 76) pensioners, 3.9% (n = 38) students, 2.8% (n = 28) farmers, 2.3% (n = 23) Merchants and 1.9% (n = 19) unemployed. Prevalence of CAM in our patients is 4.2%. **Conclusions.** In the group studied the observed prevalence is low, highlighting the female gender, use of herbal and related to digestive disorders.

* The terms used in this area were not very specific, such as soda, feel good, taste, rehydration, quality of life, decay, oxygenating, purifying and defenses.

EPIDEMIOLOGIC PROFILE OF CHRONIC HEPATIC LIVER DISEASE IN PERUVIAN-JAPANESE MEDICAL CENTER, LIMA-PERU

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Purpose. The present work aims to identify the epidemiologic profile of patients with chronic liver diseases attending outpatient consultations at our medical center. **Material and methods.** A retrospective study was carried out reviewing clinics stories of 272 patients who regularly attended the outpatient office at the Peruvian-Japanese Medical Center between years 2005 to 2011. **Results.** It was obtained the following results in relation to etiology: non alcoholic fatty liver disease 32.7% (89 cases), C hepatitis 20.5% (56 cases), alcoholic liver disease 10.6% (29 cases), B hepatitis 9.5% (26 cases), drug induced liver disease 4.4% (12 cases), primary biliary cirrhosis 2.5% (7 cases), cirrhosis plus diabetes 5.1% (14 cases) and idiopatic cirrhosis 8.4% (23 cases). When patients with non alcoholic liver disease, cirrhosis and diabetes as well as cirrhotic patients of unknown origin but with evidence of metabolic syndrom were added the figure rose to 46.2%. The 45.3% of patients with non alcoholic fatty liver disease were male with average age of 46.1 years old and body mass index of 31. Women were 54.6% in this group with average age of 55.6 years old and body mass index of 30.7. **Conclusions.** Non alcoholic fatty liver disease aside with chronic liver disease with evidence of metabolic syndrom were more frequent cause of consultations at our medical center, more common in female and in obesity patients.

HEPATOTOXICITY BY AMOXICILLIN/CLAVULANIC ACID. CASE REPORT

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Case report. 44 years old women, was admitted with 6 days of mucocutaneous jaundice development, acholia, nauseas, pruritus, without pain abdomen, no visceromegaly, afebrile and history of treatment during 20 days with amoxicillin/clavulanic acid because of a respiratory infection that was over 10 days before the symptoms began. Laboratory: WC: 6400; Hemoglobin: 12; Hematocrit: 36; Creatinine: 0,6; Alkaline phosphatase: 336; Total bilirubim: 17 g/dL; Direct bilirubim: 11 g/dL; PT: 12; KPTT: 25; HBV, HCV, HAV, HIV, EBV: negatives. ANAs, ASMAs and AMA non reactive. Ultrasonography abdominal, resonance cholangiopancreatography: normals. The histopathology of the Percutaneous liver biopsy, associated to the clinical information, matches a cholestatic hepatitis, which is most likely linked to the precedent description. The patient favorably evolves. Information update: Among penicillin, amoxicillin/clavulanic acid is the most frequent cause estimated on 10/100,000 prescriptions. It may present itself in several ways, such as nausea, vomits, abdominal pain, fiver, pruritus and jaundice. There are differences according to the age of the patient, where hepatocellular predominates in young people and, mixed/cholestatic in the elders patients. The process of this pathology is idiosyncratic. The diagnosis is done by exclusion and based mainly on clinical suspicion. Healing is the norm; however it has been described a 7% chance of adverse evolution, such as death, transplant or persistency of liver damage. It has been identified a significant association between haplotypes HLA type II with susceptibility to hepatic toxicity, however, given its low frequency and prevalence of these haplotypes in healthy controls (12%), other factors must be considered.

ADAPTATION OF A POLYMERASE CHAIN REACTION (PCR) ASSAY FOR DETECTION OF *LACTOBACILLUS RHAMNOSUS GG* (LGG) IN GUT OF ZEBRAFISH AFTER ALCOHOL EXPOSURE

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Purpose. To adapt a PCR assay to detect colonization of LGG in zebrafish after ethanol exposure. **Material and methods.** Adult wild-type zebrafish (10/group): Control (C); Probiotic (P); Probiotic + Ethanol (PE) - ethanol 0.5%. Fish were fed during 2 weeks with LGG supplemented feed (P and PE) and unsupplemented (C). Colonies isolates from gut cultures in MRS agar were picked up and resuspended. Bacterial suspension -1.0 McFarland standard - was prepared in 500 μl TE (10 mM Tris/HCl, 1 mM EDTA, pH 8.0). Suspension was homogenized and heated at 100 ºC/10 min, frozen at -80 ºC for 2 h. Nucleic acid extraction was performed (QIAamp® Viral RNA Mini Kit). Specie-specific primers were utilized. PCR amplifications conditions: final volume of 50 μl containing 5 μL the DNA, 67 mM Tris-HCl, 16 mM $(NH4)_2SO_4$, 0.01% (w/w) Tween-20 (pH 8.8 at 25 ºC), 1.5 mM $MgCl_2$, 0.25 mM dNTP, 1 pmol of each primer and 2.5 U of enzyme Super-Term. Cycling: 94 °C for 5 min followed by a touch-down thermocycling program (annealing for 30 s at 62 °C in cycles 1 to 10, at 60 °C in cycles 11 to 20, and at 58 °C in cycles 21 to 30, with extension for 1 min at 72 °C and denaturation for 40 s at 94°C), final extension for 5 min at 72 °C. PCR products were run on a 2% agarose gel in 0.5% Tris-borate-EDTA buffer. **Results.** Colonies isolates were confirmed by PCR as LGG strain. **Conclusion.** PCR assay was adequately established. Ethanol exposure does not affect the LGG colonization in zebrafish gut.

INFLUENCE OF THE ACCESS TO OWN EGGS IN SERUM LIPID PROFILE IN ZEBRAFISH *(DANIO RERIO)*

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Purpose. To evaluate the influence of accessing eggs on cholesterol and triglycerides serum levels of zebrafish. **Material and methods.** Adult zebrafish, wild type, of both genders were divided into two groups: group 1 free access to their own eggs and group 2 no access (the bottom of the aquarium was filled with glass balls to prevent them to access their eggs for two weeks). Both groups were kept fasting for 24 h before the blood collection. In order to collect the blood samples, animals were anesthetized and an incision was made in the tail to allow access to the dorsal vein. The collected blood was centri-

fuged and serum was obtained for analysis. Triglycerides and cholesterol serum levels were analyzed with colorimetric tests. The *n* used was 4 for each group. *Pools* with serum of 10 animals were used to biochemical analysis. **Results.** The results are expressed in mean ± standard error. There was a significant difference on triglycerides levels (group 1 = 457 ± 43 mg/dL and group 2 = 292 ± 111 mg/dL; P < 0,03). However, there was no significant difference on cholesterol serum levels (total cholesterol: group 1 = 362 ± 73 mg/dL and group 2 = 357 ± 23 mg/dL; HDL - cholesterol: group 1 = 91,22 ± 1,79 group 2 = 72,14 ± 2,89; LDL - cholesterol: group 1 = 55,68 ± 10,88 group 2 = 44,18 ± 9,84). **Conclusion:** The access to own eggs seems to influence the zebrafish triglycerides serum levels without modifying cholesterol serum.

ETHANOL EFFECTS ON TRIGLYCERIDES AND CHOLESTEROL SERUM LEVELS OF ZEBRAFISH *(DANIO RERIO)*

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Purpose. To evaluate the effect of ethanol on triglycerides and cholesterol of zebrafish serum. **Materials and methods.** Adult, wild type zebrafish (n = 180) were divided into 2 groups: Control (C; n = 90) and Ethanol (E; n = 90), exposed to 0.5% ethanol added to the water. Fish received commercial flake food (Tetramin Pro Care) twice a day. Blood samples were collected after 2 and 4 weeks: 45 fish of each group were euthanized by hypothermic shock. Incision was made in the tail to access to the dorsal vein. Blood samples (pool from 10 fish) were centrifuged and serum was obtained for analysis by colorimetric tests (Labtest). The *n* used was 4 for each group. Statistics: One-way analysis of variance (ANOVA) with Bonferroni test was performed to compare any significant differences ($p < 0.05$) between groups. Experimental data is presented as the mean ± standard deviations (SD). **Results.** Two weeks: Triglycerides (C) = 739.20 ± 44.03; (E) = 524.40 ± 36.86; Cholesterol (C) = 470.65 ± 44.17; (E) = 458.92 ± 39.07. Four weeks: Triglycerides (C) = 673.17 ± 44.17; (E) = 309.77 ± 39.41; Cholesterol (C) = 434.32 ± 49.62; (E) = 309.77 ± 39.41. There was a significant difference between C and E groups related to time of ethanol exposure and cholesterol ($p < 0.001$) and triglycerides levels ($p < 0.001$). **Conclusion.** Triglycerides and cholesterol levels of Zebrafish were affected by ethanol exposure.

INFLUENCE OF *ABCC2* HAPLOTYPES ON INDIOSYNCRATIC DRUG-INDUCED LIVER INJURY (DILI) SUSCEPTIBILITY

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Aims. Multidrug resistance protein 2 (MRP2, *ABCC2*) plays an important role in the biliary clearance of a wide variety of endogenous and organic anion from exogenous compounds. Therefore, polymorphisms in the *ABCC2* gene may affect individual susceptibility to hepatotoxic reactions, as demonstrated by Choi, *et al.* (2007) in a Korean population. We aimed to analyze the influence of four *ABCC2* polymorphisms on the risk of developing hepatotoxicity and the phenotypic expression. **Material and methods.** Genotyping of the *ABCC2* polymorphisms -1548G>A, -24C>T, 1249G>A and 4588G>A was performed in 94 Spanish DILI patients and 162 Spanish bone-marrow donors, serving as the control group, using the TaqMan 5´ allelic discrimination assay. Haplotype assembly and genetic associations were performed using the Haploview 4.2 program and Chi Squared test, respectively. **Results.** Individual allelic variations were analyzed, but no differences were found between DILI patients and controls. Hardy-Weinberg equilibrium was observed for all the polymorphisms. DILI patients showed a strong linkage disequilibrium (LD) between loci -1549G>A and 1249G>A (D' = 0.97), -1549G>A and -24C>T (D' = 0.90) and -1549G>A and 4581G>A (D' = 0.83). The haplotype frequencies at loci -1549/-24/1249/4581 were: GCGG (27.8%), ATGG (26%), ACGG (19.2%), GCAG (18%), ACGA (6.7%) and GTGG (1.4%). Only the GTGG haplotype showed a statistical significant difference in frequency between patients and controls (P = 0.028). However, as the frequency was below 5% it is not considered viable. In addition, the significance remained for cholestatic/mixed type of DILI when compared to controls (P = 0.042). The GTGG haplotype was not different when comparing hepatocellular DILI patients with the control group. **Conclusions.** These data do not support evidence for the ABCC2 polymorphisms -1548G>A, -24C>T, 1249G>A and 4588G>A as potential risk factors for DILI.

THE INFLUENCE OF AROMATIC SUBSTITUENTS IN THE CAUSATIVE DRUG ON THE GLUTATHIONE S-TRANSFERASE M1 AND T1 DETOXIFYING PROCESS AND HEPATOTOXICITY (DILI)

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Aims. Glutathione S-transferase (GST) is a main family of phase II enzymes, with a key role in the detoxifying process of drugs and xenobiotics. Our group has identified that the combined null genotype *GSTM1* and *T1* plays a role in the general mechanism of DILI susceptibility (Hepatology, 2008), potantially due to the presence of aromatics ring in the causative drug molecule. Lyttle, *et al. (J Med Chem*, 1994) have shown that the chemical nature of atoms or molecules replacing hydrogen atoms in the aromatic ring might interfere in the ability of GST to conjugate the substrates. We aimed to analyze whether DILI patients with the combined *GSTT1*/*GSTM1* null genotype have a higher risk of hepatotoxicity when exposed to drugs with aromatic rings in their chemical structure, and the influence of the chemical nature of aromatic substituents on the detoxifying process. **Material and methods.** One hundred fifty four diagnosed DILI patients and 250 healthy controls were analyzed. Genotyping of *GSTM1* and *GSTT1* was performed using a multiplex PCR assay. The substituents were classified as 'activating' if the ring reactivity was increased or as 'deactivating' in cases of

decreased ring reactivity. Results: The *GST M1/T1* null genotype was significantly associated with DILI in patients exposed to drugs with aromatic rings when compared to the controls (*Pc* = 0.004; OR = 3.0). The presence of activating substituents solely in the aromatic ring enhanced the risk of DILI 3.1 times (n = 54; *Pc* = 0.019). Only two patients developed DILI due to drugs with just deactivating substituents in the ring. The genotype distribution did not show any statistically significant differences when electron donor and withdrawing substituents were present simultaneously in the molecule (n = 18; *Pc* = 1.000). **Conclusions.** Patients homozygous for the *GSTM1/T1* null genotype have an increased risk of developing DILI when exposed to drugs containing aromatic rings in their chemical structures, particularly if the aromatic ring only contains electron donor substituents.

HEPATIC FASCIOLIASIS COMPLICATED BY HEPATIC VENOUS THROMBOSIS

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Purpose. To describe a case of hepatic fascioliasis complicated by hepatic venous thrombosis. **Results.** A 45 years old man from Perú, complaining of an intermittent dull epigastric abdominal pain radiated to the back, of 45 day's duration. Prior to the admission had a diagnostic of gallstones and mild chronic superficial gastritis. He was scheduled for a cholecistectomy, and the day of the surgery presented a cholestatic jaundice, coluria without other symptoms. During surgery, they found: a raised white lesion in liver segment III with a serpentine path, gallbladder with adhesions, edematous wall, containing thick dark bile and multiple small stones and a wide cystic duct. Intraoperative cholangiography was normal. Histopathologic examination revealed eosinophilic cholecystitis and necrotizing granulomatous hepatitis with predominantly eosinophilic inflammatory infiltrate. Laboratories showed eosinophilia (absolute count 1587.6 mm^3). An abdominal CT scan performed two days after surgery revealed impaired perfusion of the right posterior segments with a hypodense linear image at the level of segment VI in the liver. Due to spiking fevers (38°C), an abdominal CTscan performed seven days post-surgery, showed areas of no-contrast enhancement at liver segments V, VI, VII, VIII and the right branch of the portal vein, compatible with thrombosis and a hypodense inflammatory area in segment VI. Anticoagulation therapy was initiated. With the positive test for Fasciola (FAS2-ELISA), a history of watercress consumption was obtained and started treatment with triclabendazole (10mg/kg/daily for 2 days). The patient condition improved. Conclusion: Acute hepatic thrombosis can be a complication of hepatic fascioliasis.

MULTIPLE HEPATOTOXICITY EPISODES ARE FREQUENTLY ASSOCIATED WITH AUTOIMMUNE PRESENTATION

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Objectives. Drug-induced liver injury (DILI) is a complex condition with various clinical and pathological presentations. We have recently demonstrated that a second DILI episode induced by a different drug with regard to the first episode increases the probability of an autoimmune DILI diagnosis (Lucena, *et al*., 2011). In this study we aimed to analyze the frequency of autoimmune presentations, type of liver injury and drugs involved in a cohort of Spanish and Latin American patients, who have suffered two DILI episodes caused by the same or different drugs. **Material and methods.** The cases included in the study were retrieved from those submitted to the Spanish and Latin American DILI Registry as having experienced reexposure to the same drug or multiple DILI episodes due to different causal agents (n = 46). The cohort was analyzed for demographic, clinical and biochemical data as well as for causative pharmacological groups. **Results.** Of the 811 cases in the DILI registry 679 contained autoimmunity data, of which only 17% displayed positive autoantibody titres. However, 41% of the 46 patients with multiple DILI episodes due the same or different causal agents were found to be autoimmune positive in the second episode. In the 31 patients with reexposition to the causal agent 29% (9 cases) presented autoantibodies, 67% anti-nuclear antibodies (ANA) and 33% anti-smooth muscle antibodies (ASMA). In comparison, in 15 patients with two DILI episodes due to different causal agents 67% (10 patients) were found to have positive autoantibodies, mainly ANA, in the second episode. Hepatocellular damage was the most prevalent type of injury in both groups and remained in both episodes. The pharmaceutical groups associated with positive autoantibodies were mainly cardiovascular system drugs (especially statins) and antibiotics. **Conclusions.** The probability of presenting positive antibody titres increases in second DILI episodes, independent of the causal agent being the same or different to that in the first episode. Statins is the pharmacological group associated with the highest risk of developing positive autoantibodies during a second DILI episode. These drugs may produce a breakdown of immune tolerance that is able to trigger liver autoreactivity.

CONCORDANCE BETWEEN HEPATIC TRANSIENT ELASTOGRAPHY BY FIBROSCAN® AND FIBROMETER® TO THE STAGE OF LIVER FIBROSIS

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Objective. The association of hepatic transient elastography by FIBROSCAN® (FS) and non invasive biomarkers of liver fibrosis, as FIBROMETER® (FM), has demonstrated usefull to increase the acuracy of these methods, when comparated to liver biopsy. This is particularlly true whe are evaluated intermediate stages of fibrosis (clinically significant fibrosis or F2). As demonstrated in French studies, the concordance between these two types of non invasive methods can exclude the need of liver biopsy to stage fibrosis in patients with chronic hepatitis C. The objective of this study is to evaluate the percentual of concordance between FIBROSCAN® and FIBROMETER® and possible factors related to theire discordance. **Material and methods.** Was defined as reliable exam by the FS, following the manufacturer instructions, at least 10 valid mesurements (as data from the equipment), 60% of valid

mesurements, interquartil range (IQR) less than 30% of valid mesurements mediana. The exams considered reliable were reclassified as much reliable (IQR < 10%), reliable (IQR 11-20%) and less reliable (IQR 21-30%). The invalid exam was determined by the softwear of the equipment. All patients were, initially submited to the exam with M probe. If this was not reliable or invalid, the patients were reexamined with XL probe. **Results.** 51 patients submited to FS and FM, in the same day, from february 2011 to march 2012 were included in the analysis, 27 (50,8%) males, with mean age of 51,7 years (28,0-80,0), diagnosis of hepatitis C in 46 (90,2%), hepatic steatosis 3 (5,9%), hepatitis B 2 (3,9%). 42 (82,4%) patients were submited to the exam to follow up of previous biopsy and 9 (17,6%) to initial diagnosis. The mean body mass index (BMI) was 25,8 kg/m^2 (18,9-41,3). The XL probe use was necessary in 6 cases (11,8%) and the mean exam duration was 3,0 min (2-10). No patient had invalid or non reliable exam by FS. When reclassified the reliable exams the distribuition was: much realiable 20 (39,2%), realiable 25 (49,0%) and les realiable 6 (11,8%). The stages of fibrosis by FS were: F0 11 (21,6%), F0-1 14 (27,5%), F1-2 10 (19,6%), F2 2 (3,9%), F3 4 (7,8%), F3-4 2 (3,9%), F4 8 (15,7%). To FM were: F0-1 8 (15,7%), F1-2 23 (45,1%), F2 6 (11,8%), F3 12 (23,5%), F3-4 1 (2,0%) F4 1 (2,0%). The concordance between FS and FM was oserved in 37 (72,5%) patients. We compare between concordants and non concordants: age, gender, diagnostic, exam indication, BMI, torax circunference, abdome circunference, wrist circunference, exam duration, type of probe, grade of realibility, fibrosis stage. Only the grade of realiability shown a tendence of statistical significance, related to concordance between FM and FS (much reliable = 90% of concordance, realiable = 60% of concordance, less realiable = 66% of concordance; P = 0,077). A FS result much realiable had high concordance with FM result. Among 13 cases of discordance, in 9 (69,2%) the FM result was one stage less than the FS. In two cases we observed discordance in more than two stages os fibrosis. In 11 (84,6%) patients the discordance was next to stage F2. **Conclusion**: We observed concordance between FM and FS in 72,5% of cases. The concordance was higher when the FS result was much reliable. Most discordance ocurred in intermediate stage of fibrosis.

REALIABILITY AND VALIDITY OF HEPATIC TRANSIENT ELASTOGRAPHY BY FIBROSCAN® USING PROBES M AND XL IN BRAZIL

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Objective. Hepatic transient elastography (FS) is a non invasive method to evaluate the stage of liver fibrosis. This technic had extense validation to chronic hepatitis C and had as gold-standard the liver biopsy. FS was, initially, discribed with M probe, but a significant number os tests were not valid or not realiable with this device. It was frequent in patients with higher body mass index (BMI). Recently, the XL probe showed a higher chance to obtein a realiable test and less chance to invalid tests. The objective of this study was evalaute realibility and validity of FS with M and XL probes. **Material and methods.** Was defined as reliable exam by the FS, following the manufacturer instructions, at least 10 valid mesurements (as data from the equipment), 60% of valid mesurements, interquartil range (IQR) less than 30% of valid mesurements mediana. The exams considered reliable were reclassified as much reliable (IQR < 10%), reliable (IQR 11-20%) and less reliable (IQR 21-30%). The invalid exam was determined by the softwear of the equipment. All patients were, initially submited to the exam with M probe. If this was not reliable or invalid, the patients were reexamined with XL probe. **Results.** 175 patients submited to FS from February 2011 to March 2012 were included in the analisis, 89 (50,8%) males, with mean age of 55,0 years (28,0-83,0), diagnosis of hepatitis C in 154 (88,0%), hepatic steatosis 11 (6,3%), hepatitis B 7 (4,0%), alcohol 2 (2,1%), hemochromatosis 1 (0,6%). 152 (86,9%) patients were submited to the exam to follow up of previous biopsy and 23 (13,1%) to initial diagnosis. The mean body mass index (BMI) was 23,8 kg/m^2 (17,5-43,3). The XL probe use was necessary in 22 cases (14,7%) and the mean exam duration was 3,0 min (2-10). Only in two cases (BMI of 37,0 and 38,9) the exam was invalid (1,1%) and in only 1 (BMI of 30,0), not realible (0,6%). When reclassified the reliable exams the distribuition was: much reliable 39 (22,7%), reliable 98 (57,0%), and les realiable 35 (20,3%). The stages of fibrosis by FS were: F0 37 (21,5%), F1 33 (19,2%), F2 34 (19,8%), F3 24 (13,7%), F4 44 (25,6%). We grouped patients with results much realiable and realiable 137 (79,7%) to compare variables with the group of patients with less realiable tests 35 (20,3%). We compare between concordants and non concordants: age, gender, diagnostic, exam indication, BMI, torax circunference, abdome circunference, wrist circunference, exam duration, type of probe, grade of realibility, fibrosis stage. Only the duration of exam less then 3 min had sattistical significance related to better realiabilidity of the exam (P = 0,029). **Conclusion.** FS had a low frequency of invalid or unrealiable exams, when using the M and XL probes sequentialy. Only the exam duration less then 3 minutes was correlated with more realiability, probably explained by the easier technical factors are generate faster exams.

VIGILANCIA DE LOS HIJOS DE MADRES POSITIVAS AL ANTÍGENO DE SUPERFICIE DE HEPATITIS B (HBSAG), CUBA, 2000-2011

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Objetivo. El riesgo de infección perinatal entre niños de madres positivas al antígeno de superficie de hepatitis B (HBsAg) es elevado. Estas infecciones pudieran prevenirse si las embarazadas positivas son detectadas precozmente y sus hijos son vacunados al nacer. La vacunación contra la hepatitis B (HB) y la administración de inmunoglobulina humana anti-HB se consideran medidas preventivas para estos niños. Este estudio es parte del Programa de Vigilancia que desde hace 20 años se realiza en Cuba para el control perinatal de la HB en hijos de madres HBsAg(+) y sus objetivos son: investigar los marcadores HBsAg y los anticuerpos contra el HBsAg (anti-HBs) en los hijos de siete y 18 meses de edad, determinar los Títulos Promedios Geométricos (TPG) de los anti-HBs, la seroprotección alcanzada, la calidad de la respuesta y conocer el Índice de Eficacia de la vacuna cubana Heberbiovac-HB®, en ambos grupos de niños. **Material y métodos.** Desde Septiembre 2000 hasta Diciembre 2011 se investigaron 488 muestras de sueros de hijos madres HBsAg(+) de siete y 18 meses de edad de todo el país recibidas en el Laboratorio Nacional de Referencia de Hepatitis viral, IPK. Además se estudiaron 174 sueros de hijos de madres HBsAg (+) a los siete y 18 meses que se les administró inmunoglobulina humana anti-HB cubana

(Ganmahep B) y vacuna cubana Heberbiovac-HB®, antes de las 12 horas de nacidos. Todos los niños fueron evaluados con los marcadores HBsAg y anti-HBs. **Resultados.** En los niños de siete meses se obtuvo 6.50% de positividad a HBsAg, los TPG de anti-HBs fueron 345.8 UI/L y la eficacia de la vacuna osciló entre 90% y 93.3%. El 3.03% fue HBsAg(+) a los 18 meses, el TPG de anti-HBs fue 390.7 UI/L y la eficacia de la vacuna osciló entre 95% y 96.7%, predominaron los hijos normo-respondedores en ambos grupos. En el grupo de niños que se le administró gammaglobulina y vacuna se encontró que a los siete meses 1.1% fue HBsAg(+), la seroprotección fue de 89.5%. El 3.4% fue HBsAg(+) a los 18 meses, con 97.6% de seroprotección. Predominó la normo-respuesta en los dos tiempos. Los TPG fueron 168.66 UI/L y 175.62 UI/L respectivamente. **Conclusiones.** La estrategia seguida en este grupo de lactantes de riesgo es satisfactoria para disminuir la transmisión perinatal.

ECHINOCOCCUS VOGELI, CAUSA POCO FRECUENTE DE EQUINOCOCCOSIS HEPÁTICA EN LA ARGENTINA. REPORTE DE UN CASO CONFIRMADO POR BIOLOGÍA MOLECULAR

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Introducción. El *Echinococcus vogeli* causa equinococosis poliquística (PE) en seres humanos en América Central y del Sur. El *echinoccus granulosus* (EG) es el principal responsable de la equinococosis quística (CE) en América del Sur. En los países endémicos para CE, el PE se diagnosticaría erróneamente como una presentación atípica de la CE o una equinococosis alveolar (EA). Se describe un caso de PE en un paciente procedente de Paraguay, hospitalizado en la Argentina, con diagnóstico inicial de CE atípica o una EA. Las técnicas moleculares aportaron pruebas para un PE. **Caso clínico.** Un inmigrante de 37 años de edad, de Paraguay, fue hospitalizado en nuestro hospital por obstrucción biliar alta por un tumor hepático central (segmentos IV y VIII). Fue tratado con un drenaje biliar percutáneo izquierdo con abscedación secundaria de la lesión, al drenarse se biopsió. La biopsia reveló la presencia de escólex (pero con ganchos de pequeño tamaño) y la serología para CE serología, DD5, ELISA, Western Blot, fue positiva. La presencia de capas parasitarias del quiste y la serología positiva hicieron presumir una AE o un CE atípico. El tratamiento con albendazol (800 mg/día) fue instituido. Debido a la persistente supuración se efectuó una segmentectomía atípica de segmentos IV y VIII, a los siete meses de su internación. La presencia de una fístula biliar y las vías biliares derechas aisladas del colédoco llevó a efectuar una hepatectomía derecha. El paciente falleció dos años más tarde con una neumonía con anti-VIH+. Se extrajo el ADN a partir la inclusión en parafina de la biopsia. La amplificación y la secuenciación de un fragmento de 155 pb del citocromo oxidasa mitocondrial b, llevó a identificación de *E. Vogeli*, con diagnóstico de EP. **Discusión.** Este es el segundo caso de diagnóstico efectuado por técnicas de biología molecular, y el primer caso probado descrito en la Argentina y Paraguay. Este caso pone de manifiesto la posible confusión entre la CE atípica, EA, EG, PE y tumores en áreas de alta endemicidad del EG. La PE tiene que ser sospechada en un paciente procedente de la zona endémica para *E. Vogeli*, que presenta varias capas en la pared del quiste, escólex, serología altamente positiva para EC, con ganchos de menor tamaño. La biología molecular permite su diagnóstico diferencial.

ENTIDADES CLÍNICAS ASOCIADAS A DUCTOPENIA-PERIODO 2007 AL 2011-LIMA-PERÚ

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Objetivo. Conocer las entidades clínicas asociadas a ductopenia, definida como la ausencia del conducto biliar principal en 50% o más de los espacios portas, de una biopsia hepática adecuada. **Material y métodos.** Se estudiaron 102 biopsias (aguja y escisión en cuña) las biopsias se fijaron con formol a 10%, procesadas y coloreadas con H-E, PAS, tricrómica de Masson, Perls y CK7. Se consideraron biopsias adecuadas aquéllas con más de once espacios portas. Se evaluaron las secciones por microscopia óptica en forma simultánea por dos patólogos. **Resultados.** En 20.5% de las biopsias la ductopenia se asoció a esteatohepatitis, 19% a cirrosis biliar primaria, en 16% de las biopsias con ductopenia no se pudo determinar la etiología, 15.6% se asoció a hepatitis autoinmune sobreposición con cirrosis biliar primaria, mientras que 12.7% se asoció a virus de hepatitis C. **Conclusión.** La ductopenia puede asociarse a una serie de entidades clínicas, entre ellas a esteatohepatitis, cirrosis biliar primaria, virus de hepatitis C y enfermedades autoinmunes.

EVALUACIÓN INTENCIONAL DEL NIVEL DE TRANSAMINASAS EN UNA POBLACIÓN DE LIMA CON RIESGO DE HEPATOPATÍA

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Introducción. La elevación de los niveles de transaminasas indican inflamación hepática y en el Perú no existen datos de lo que ocurre en la población general. El presente estudio tiene por finalidad determinar con qué frecuencia se encuentra elevación de transaminasas en una muestra intencionada de la población y si ello tiene relación con algún factor epidemiológico. **Material y métodos.** Se aplicó una encuesta epidemiológica a quienes voluntariamente aceptaron participar entre los asistentes a una campaña de prevención en hepatitis, realizada el 19 de mayo 2009 en el HNERM-EsSalud. Esto permitió identificar al menos un factor de riesgo para hepatopatía, y en estos casos se analizaron los niveles de transaminasas. Se realizó un análisis estadístico descriptivo y la prueba de χ^2. **Resultados.** Se encuestaron a 281 personas, de ellas 231 tuvieron al menos un factor de riesgo para hepatopatía: antecedente de hemotransfusión, antecedente de hepatitis, contacto con persona con hepatitis, tatuaje, piercing, consumo de alcohol y ser portador de diabetes o dislipidemia. Se consideraron válidas a 225. La edad media fue de 53.7 ± 15.55 años, TGO 29.12 ± 16.09 UI/mL, TGP 31.72 ± 24.94 UI/mL, IMC 26.52 ± 4.08. El 15.6% reportó tener hipertensión arterial, 13.3% padeció hepatitis, 19.1% recibió hemotransfusión; contacto con persona con hepatitis 29.3%; portador de piercing 7.9%, portador de tatuaje 2.2%, consumo de alcohol 39.6%, diabetes mellitus 6.7% y portador de dislipidemia 40.9%. Del total de personas evaluadas, 29.7% presentó elevación de TGO y

20.4% elevación de TGP. En conjunto, 31.1% presentó transaminasas elevadas. En relación con el IMC, 51.1% presentó sobrepeso y 14.2% obesidad. En el análisis bivariado, la elevación de transaminasas fue más frecuente en varones que en mujeres (36 *vs.* 28.7%). De todas las variables analizadas, únicamente el nivel de IMC se asoció en forma significativa a la elevación de transaminasas ($p < 0.001$). **Conclusiones.** Éste es el primer estudio a nivel nacional que demuestra elevación de transaminasas hasta en 31.1% de personas; el factor de riesgo más importante fue el sobrepeso/obesidad. Dado que fue un muestreo intencionado en una población no seleccionada de Lima, el sesgo de selección está presente por lo que los resultados no son concluyentes. Aun así, este estudio puede servir de base para un estudio más extenso de la enfermedad hepática en el Perú.

RATOS DIABÉTICOS TRATADOS COM DIFERENTES DOSES DE ÔMEGA3 E SEUS EFEITOS SOBRE PARÂMETROS METABÓLICOS E OXIDATIVOS

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Objetivo do trabalho foi avaliar o efeito da administração de duas doses de ômega 3 sobre o dano oxidativo e a atividade da superóxido dismutase no fígado, rim e intestino de ratos diabéticos. **Material e métodos.** O diabetes foi induzido em ratos machos Wistar através da injeção intaperitoneal de estreptozotocina na dose de 70 mg/kg de peso. Foram avaliados os níveis glicêmicos e o tratamento foi iniciado 72 horas após a indução. Os animais foram tratados com ômega3 na dose de 1 g/kg e 4 g/kg através de gavagem. Os animais foram divididos em 8 grupos: CO receberam solução fisiológica; CO+O15; CO+O30: receberam ômega3 na dose de 4 g/kg durante 15 e 30 dias respectivamente; CO+O(1): receberam ômega 3 na dose de 1g/kg durante 30 dias; DM: receberam solução fisiológica; DM + O15; DM + O30: receberam ômega 3 na dose de 4 g/kg durante 15 e 30 dias respectivamente e DM+O(1) receberam ômega 3 na dose de 1 g/kg durante 30 dias. Após o tratamento, os animais foram anestesiados e foi retirado sangue do plexo reto-orbital para análise da glicemia, triglicerídeos e colesterol. O fígado, o rim e o intestino foram retirados, congelados e armazenados para as análises bioquímicas. A análise estatística foi ANOVA seguida de teste de Student-Newman-Keuls, foi considerado diferença significativa quando o $p < 0,05$. **Resultados.** O tratamento com ômega 3 não melhora a glicemia mas é capaz de reduzir a perda de peso nos animais diabéticos e provocar uma redução nos TG após 30 dias de tratamento com ambas as doses. No fígado, os animais diabéticos e os tratados com ômega nas duas doses apresentaram aumento no dano oxidativo, porém os animais tratados com 4 g/Kg de ômega 3 durante 15 dias e os tratados durante 30 dias com 1 g/Kg de ômega 3 mostraram aumento na atividade da SOD. Os animais diabéticos tratados com ômega 3 apresentaram uma redução no dano oxidativo que no rim, foi mais efetiva na dose de 1 g/kg enquanto no intestino foi melhor na dose de 4g/kg. No rim dos animais diabéticos não houve modificação na atividade da SOD, porém no intestino o tratamento com 1 g/kg aumentou significativamente a atividade da SOD. **Conclusão.** O tratamento com ômega 3 foi capaz de reduzir o dano oxidativo e aumentar a atividade da SOD, porém esta resposta foi variável com o tecido e com a dose de ômega 3 utilizada.

LIVER SURGERY AND LIVER TRANSPLANTATION

EXPERIENCE OF ORTHOTOPIC LIVER TRANSPLANTATION (OLT) AS A TREATMENT IN HEPATOCARCINOMA (HCC)

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Introduction. HCC is a major cause of death in cirrhotic patients. The OLT is one of the potentially curable treatments. The main aim was to estimate the survival rates after OLT.

Table 1. Survival post transplantation: global, MELD scores, AFP levels and Child-Pugh scores.

Survival post OLT (years)	1	3	5	P value
Global	80%	68%	45%	
MELD ≤ 18	70%	70%	45%	0.02
MELD > 18	100%	50%	25%	
AFP ≤ 400 UI/dL	80%	80%	75%	0.02
AFP > 400 UI/dL	80%	40%	0%	
Child A-B	75%	75%	50%	0.2
Child C	100%	38%	0%	

Material and methods. A retrospective study was performed, during a period of 13 years, from patients with confirmed diagnosis of HCC that were undergoing to OLT at one center. The survival rate was estimated through Kaplan-Meier. **Results.** A total of 188 OLT were performed during a 13-year period, of which 16 occurred in patients with HCC, 13 men (81.3%), three women (18.7%), aged 55,9 ± 7.8 years old. All patients had chronic liver damage (CLD), 12 of which were classified as Child A-B group. The main aetiology for CLD was hepatitis C virus (HCV; five cases). The model for end liver disease score (MELD) averaged 15.4 ± 4.3. Mean values of AFP were 2079 IU/dL. Fourteen patients met the Milan criteria. PreOLT therapies were: alcoholization (2), chemoembolization (2), radiofrequency ablation (5), and surgery (4). Only 6 patients did not receive treatment prior to transplantation. The mean elapsed time between the diagnosis of CLD and HCC was 4.5 ± 3.7 years. **Conclusions.** The predominant diagnostic of CLD was HCV. The OLT had a survival rate of 60% during the first three-year post transplantation. In this study, the patients with longer survival were those in which the AFP levels were ≤ 400 IU/dL. The small number of patients can be explained by the prolonged time on the waiting list because many of them drop out of the transplantation criteria.

TACROLIMUS *VS.* CYCLOSPORINE AS PRIMARY IMMUNOSUPPRESSION AFTER LIVER TRANSPLANTATION IN CHILEAN PATIENTS

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Purpose. We evaluated results and survival from a prospective trial that compared Tac and CsA-me for primary immunosuppresion. **Material and methods.** From 2002 to 2010, 143 liver transplantation from cadaveric donors were performed at the Hospital Clínico Universidad de Chile. One hundred

thirty one (91.1%) received CsA-me or generic tacrolimus (T-Inmun®) as primary immunosuppression. We evaluated clinical variables and the survival of these patients. Statistical analysis was performed with Stata 10.0. **Results.** Eighty one (60.0%) received CsA-me and fithy four (39.3%) received Tac. Median age was 52.9 (21-68) years, not differences for sex. Causes for transplantation in CsA-me group was HCV 30.0%; alcoholic cirrhosis 20.0%; NASH 12.5%; cryptogenic cirrhosis 8.8%; other 28.7% and in the Tac group: NASH 24.5%; alcoholic cirrhosis 15.1%; cryptogenic cirrhosis 13.2%; autoimmune hepatitis 11.3% and other 35.8% (p = ns by group). Patient Survival analysis of group CsA-me were 83.4%, 67.7% and 56.7% at 1,3 and 5 year, respectively, on group Tac were 93.9%, 91.6% and 86.5% respectively (log rank $p < 0.0001$). The infections (16.0% v/s 1.8%) and moderate and severe graft rejections (17.2% v/s 11.1%) were more frequent at CsA-me group ($p < 0.02$). No differences in relation to acute kidney failure and de-novo insulin-requiring diabetes mellitus were seen. **Conclusions.** Tac has superior to CsA-me in improving survival (patient and graft) and preventing acute rejection in liver transplantation. Tacrolimus seems to be a more appropriate drug to be used for primary immunosuppression in Chilean liver transplantation.

IMPACT OF CREATININE VALUES ON MODEL FOR END-STAGE LIVER DISEASE (MELD) SCORES IN MALE AND FEMALE CANDIDATES FOR LIVER TRANSPLANTATION

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Purpose. A systematic bias against women, resulting from the use of creatinine as a measure of renal function, has been identified in MELD-based liver allocation. Correction of this bias by calculation of female creatinine levels using the MDRD formula or by re-weighting the components of the MELD score for greater emphasis on total bilirubin has been suggested. **Material and methods.** A cohort of 639 cirrhotic candidates for first-time liver transplantation was studied. Creatinine levels were corrected for gender using the MDRD formula. The accuracy of MELD and re-weighted MELD, with or without creatinine correction, to predict 3 and 6-month mortality after inclusion in a transplant waiting list was estimated. **Results.** Women exhibited significantly lower creatinine levels, glomerular filtration rate, and MELD and re-weighted MELD scores than men. After creatinine correction, female MELD scores had a mean increase of 1.1 points. Creatinine correction yielded an increase of 3 points in the MELD score in 15.2% of patients, 2 points in 22.4%, and 1 point in 17.6% of patients. Creatinine correction of reweighted MELD yielded a mean increase of 0.14 in the score, with no change in the score in 67.6% of female patients. **Conclusions.** The accuracy of MELD and re-weighted MELD, with or without correction, for prediction of 3 and 6-month mortality was similar.

RISK OF TRANSMISSION OF HEPATITIS B VIRUS FROM ANTI-CORE POSITIVE LIVER DONORS. A MULTICENTER STUDY IN ARGENTINA

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Introduction. As a result of the disparity between number of donors and patients on the waiting list for liver transplantation, resources should be optimized. The use of anti-HBc (+) donors is a strategy that has been evaluated in recent years. **Objective.** To assess the use of anti-HBc (+) liver grafts, characteristics of recipients, prophylactic strategy and post transplant hepatitis B evolution. **Material and methods.** We evaluated donors processes opened from January 2005 to July 2011 from anti-HBc (+) donors in our country, reported in INCUCAI database. We compared the characteristics of implanted and discarded donors. Then we selected 5 centers more anti-HBc+ liver grafts implanted to assess the evolution of the receptors. **Results.** 116 anti-HBc (+) donating processes were reported for liver transplantation, of which 47 were implanted, constituting 2.8% of 1693 cadaveric liver transplants performed in adults during the evaluation period. Regarding implanted and discarded organs characteristics the only significant difference was TGP level (25 ± 16 *vs.* 50 ± 59 UI/L). We evaluated 40 receptors. Their mean age was 55 ± 10 years. MELD score: 25 ± 10. Indication for transplant: HCV (9), ALD (8), HBV (6), other (17). Hepatocellular carcinoma was present in 9 patients at the time of transplant. The mean follow up was 32 ± 20 months. There were 4 cases of *de novo* HBV at 19, 24, 25 months post transplant respectively. No graft losses were observed in these patients. None of them had received prophylaxis and had no previous contact with HBV. **Conclusion.** This study demonstrated the absence of de novo hepatitis B in patients transplanted with anti-HBc (+) grafts receiving different HBV prophylaxis strategies. These results should encourage greater use of anti-HBc (+) liver grafts.

LIVER RETRANSPLANTATION: RESULTS OF A CENTER IN COLOMBIA

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Objectives. Orthotopic liver transplantation (OLT) is the treatment of choice for acute and chronic liver failure. Liver retransplantation is the only therapeutic option for graft-failure. Constitutes 5 to 23% of all transplants. It is related to increased complications, costs and less patient survival. The objectives are evaluated the incidence of liver retransplantation, describe the complications and survival of patients in the series of OLT in Pablo Tobon Uribe Hospital and University of Antioquia transplant group in Medellin, Colombia. **Material and methods.** Retrospective descriptive study of 272 OLT performed in adults from April 2004 to December 2010. **Results.** Liver retransplantation was performed in 21 patients (7.7%). The average age was 49 years and 76% were men. The main indications were hepatic artery thrombosis, ischemic cholangiopathy and chronic rejection. Survival of patients at 1 year was 81% and at 5 years was 76%, with graft survival at 1 year 76% and 5 years 72%. Bleeding was present in 3 patients (14%). Vascular complications were documented in 4 patients, one with hepatic artery thrombosis. Biliary complications occurred in 4 patients (19%). Infections were found in 11 patients (52%), being the most frequent cause abdominal bacterial infections. Acute rejection was present in 6 patients (28%) and chronic rejection in 1 patient. The main cause of death was primary graft dysfunction in 3 patients. **Conclusion.** Liver retransplantation is a complex procedu-

re requiring great technical skill and more complications are present than in a first transplant. In our series, retransplantation occurred in less than 10% of the transplanted patients, the main indication was hepatic artery thrombosis and survival at 5 years was greater than 70%.

INMEDIATE EXTUBATION IN ADULTS UNDERGOING LIVER TRANSPLANTATION: ITS IMPACT ON POSTOPERATIVE MORTALITY

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Currently, there is no method that allows us to predict which patients will need ventilatory support after liver transplantation. This reinforces the idea that all patients need to be ventilated after surgery. The aim of our study was to evaluate the impact of time of extubation on early mortality in patients who have undergone liver transplantation. We have also studied the influence of a number of perioperative variables on extubation outcome. The study was divided into three groups: one in which extubation was performed in the operating room (inmediate extubation), another for the first 24 h (early extubation) and another where extubation was performed after 24 h (late extubation). Mechanical ventilation is essential in the management of patients who have undergone liver transplantation, up to date there is no consensus on choosing the best time to extubate this patient group. The aim of our study was to evaluate the impact of early extubation in a large group of patients who received a liver transplant. To do this, we compared, retrospectively, three groups, one of early extubation (in the postanesthesia resuscitation area), within 24 h and longer (after 24 h).We excluded patients with hepatorenal transplant, fulminant hepatitis and those who were aged less than 16 years. The results of the pre-and posttransplant factors evaluated are summarized in table 1 (mean ± SD). In the logistic regression model, the APACHE II score ≥ 14 during the first 24 h of admission to the intensive care unit after transplantation was an independent predictor of late extubation (OR 8.3 CI 2.5-27.4). Hepatic encephalopathy pretransplant had an OR 3.5 (CI 0.9-12.6) as independent predictor of late extubation. Our results demonstrate that early extubation is deemed to be more feasible in patients with lower MELD and APACHE II score with less encephalopathy and better renal function. Early extubation was associated with better survival in the immediate posttransplant. In the future strategies need to be designed in order to extubate recipients from liver transplantation faster.

ONCE-DAILY TACROLIMUS EXTENDED RELEASE FORMULATION: A HEMODYNAMIC STUDY IN STABLE LIVER TRANSPLANT PATIENTS

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In recent years, it has been shown that one of the ways to improve compliance with immunosuppressive drugs may be the use of regimens that require less frequent dosing. In this regard, a once-daily extended release formulation of tacrolimus has been developed that allows a 1:1 conversion from the twice-a-day tacrolimus formulation. Moreover, pharmacokinetic and clinical studies have shown the safety and effectiveness of this conversion. Until now, it has not been assessed whether the clinical parameters are associated with a hemodynamic correlation in these patients. The aim of the present study was to study systemic, renal and splanchnic hemodynamic parameters of a switch to tacrolimus extended-release formulation (TAC-ER). Therefore, cardiac output and portal blood flow were measured by Doppler technique in 8 stable liver transplant recipients. Patients were converted, at least 6 months after transplantation, to TAC-ER on a 1:1 (mg:mg) basis for their total dose, and were maintained on a once-daily am dosing regimen for two months before hemodynamic assessment. From the clinical point of view, the conversion was accompanied by no rejection episode and similar creatinine values, blood glucose and mean arterial pressure. Measurements of systemic, renal and splanchnic parameters, preconversion and TAC-ER are (Mean ± SD): mean arterial pressure (mmHg) 104 ± 10 *vs.* 100 ± 8, cardiac output (l/min) 5.0 ± 0.7 *vs.* 4.9 ± 0.8, peripheral vascular resistance (dyne.sec.cm^{-5}) 1,680 ± 280 *vs.* 1,640 ± 320, portal blood flow (mL/min) 1,489 ± 448 *vs.* 1,520 ± 520, pulsatility renal index 0.8 ± 0.1 *vs.* 0.8 ± 0.2. No significant differences were observed between both groups. Our results show, as well as published clinical studies, the conversion to TAC-ER is safe and effective in stable patients after liver transplantation. Furthermore, we demonstrate for the first time that the conversion to TAC-ER was not associated with changes in systemic, renal and splanchnic hemodynamic parameters. This is probably the hemodynamic expression that the conversion is not associated with impaired renal function or arterial hypertension in this group of patients.

ARTIFICIAL LIVER SUPPORT SYSTEM "MARS®-PRISMA®". EXPERIENCE IN INTENSIVE CARE UNIT OF A TERTIARY HOSPITAL WITH A LIVER TRANSPLANT PROGRAM

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Table 1. Inmediate extubation in adults undergoing liver transplantation: Its impact on postoperative mortality.

	Inmediate extubation (n = 19)	Early extubation (n = 43)	Late extubation (n = 33)
MELD score	15±7	16±6	22 ± 10*
Encephalopathy (%)	5 (1-26)	21(10-36)	45 (CI 28-63)*
Creatinine (mg/dL)	0.8±0.2	0.9±0.6	1.3 ± 0.9*
APACHE II	11±5	11±4	16 ± 5*
Vasopressors > 72 h (%)	-	-	36 (CI 20-54)*
Respiratory infection (%)	-	-	24 (CI 11-42)*
Mortality (%)	-	7(1-19)	18 (CI 7-35)*

* P < 0.05.

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Purpose. To assess the efficacy of the Molecular Adsorbent Recirculating System MARS® in patients with acute severe liver failure (ASLF). **Material and methods.** Descriptive study was performed in adults with ASLF treated with MARS®-PRISMA® in an ICU of a tertiary hospital with liver transplant (LT) program. Period of study: 2003-2011. The analyzed variables were: Clinical situation,severity scores calculated during the first 24 h of ICU admission (APACHEII; SAPSII, SOFA, CHILD-PUGH and MELD Score), hemodynamic parameters, liver function tests, coagulation, plasma electrolytes, hemogram were performed before and at 4, 8, 24, 32 and 48 h after the MARS® started. Adverse events (AE) were evaluated during therapy. Length of stay (in ICU and in hospital) and mortality were analized. **Results.** 65 treatments with MARS®-PRISMA® were performed (205 sessions on the 60 patients). The etiology of ASLF was:acute liver failure (ALF) in 14, graft dysfunction (GD) after LT in 38, acute-on-chronic liver failure (AoCLF) in 10, and other etiology in 4 patients. Mean age 53 ± 14 years, males 53. APACHE II 16,34 ± 8,3; SAPS II 40,48 ± 18,22; SOFA 10,56 ± 2,94; CHILD-PUGH 11,4 ± 1,71; MELD 29,87 ± 8,22. Significant improvement of serum bilirubin, transaminases and serum ammonium were observed in the first 24 h after MARS® therapy. MARS® was well tolerated in all cases, with no AE. Twenty seven patients underwent LT. Waiting time for LT was nine days. ICU and Hospital stay median were eight and forty two days respectively.ICU mortality was 29.23%. ICU mortality was lower for patients that could receive a LT (26% *vs.* 32%) **Conclusions.** 1. MARS® seems to be effective therapy for ALF patients, as a bridge to LT. 2. MARS® not increase the waiting time for LT. 3. MARS® could be useful in patients with GD until liver regeneration. 4. MARS® can be applied in an ICU setting to patients without significant AE.

COMBINED HORMONAL RESUSCITATION PROTOCOL (METHYLPREDNISOLONE AND TRIIODOTHYRONINE) DECREASES ISCHEMIA-REPERFUSION LIVER INJURY

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Purpose. Solid organ trasplantation process is not exempt of graft damage, which is related to donor status prior procurement, graft quality, cold ischemia time extension and reperfusion in the recipient. Combined hormonal resuscitation protocols were initially developed to keep brain death donor hemodinamycally stable and pursue cardiac graft benefit as a primary aim and secondarily, maintain an effective perfusion of other organs. The purpose of this study was to determine the effect of a combined protocol of methylprednisolone (MP) and triiodothyronine (T_3) over warm ischemia-reperfusion (IR) liver injury. **Material and methods.** Male Sprague Dawley rats received a single ip. injection of 0,34 mg/kg of MP and/or 0,05 mg/kg of T_3 or its vehicles (vMP and/or NaOH) prior 1h of warm ischemia and 3 h of reperfusion. Serum and tissue samples were taken at the end of reperfusion for injury and oxidative stress parameters determinations. **Results.** Combined MP+T3, and each single drug pretreatment decrease AST/ALT serum levels, from 55 to 98% in T_3 and MP groups ($p < 0,05$, one way ANOVA). Necrosis area and inflammation evaluated by histology decrease in MP+T_3 groups, as well as oxidative stress studied by carbonylated protein levels. **Conclusions.** The combined protocol MP+T_3 in this preclinical study protects liver tissue against IR injury, decreasing serum injury biomarkers and liver necrosis and oxidative stress; which support the use of this strategy in potential liver donors.

PROGNOSTIC FACTORS ASSOCIATED WITH MORTALITY AFTER LIVER RETRANSPLANTATION: EXPERIENCE FROM A CENTER IN SOUTHERN BRAZIL

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Introduction. Survival after liver transplantation has steadily increased. In irreversible graft failure, liver retransplantation (LRT) is the only treatment option, but it is associated with worse outcomes. **Objectives.** To evaluate the association of donor, recipient and perioperative period characteristics with 1 year mortality after LRT by the Liver Transplantation Group, Santa Casa de Misericordia de Porto Alegre, Brazil. **Material and methods.** We retrospectively included patients undergoing LRT between August 1997 and August 2011. Eighteen recipient variables, six donor variables and seven perioperative period variables were studied. We also evaluated the occurrence of gender and ABO group identity, age difference between donor and recipient and D-MELD. We made a univariate analysis using chi-square or Fisher exact test for categorical variables and Student t test or Mann-Whitney test for continuous variables. **Results.** Forty patients underwent 42 retransplantation, 5% of all transplants performed. Two patients underwent two regrafts. The mean age of patients was 48.8 years and 69% were male. Hepatitis C and hepatic artery thrombosis were the most common indications for transplantation and LRT, respectively. The mean follow-up was 2.8 years. In the first year after LRT, twenty-three transplants were associated with recipient death, whose most frequent cause was septic shock. We found a significant association between 1 year mortality and the following variables: hepatitis C infection, albumin, mechanical ventilation before LRT, male donor and platelet transfusion during surgery. **Conclusion.** LRT is associated with high mortality. Identification of patients at high risk of unfavorable outcomes is important in trying to get better results.

PREDICTOR VALUE OF D-MELD ON MORTALITY AFTER LIVER RETRANSPLANTATION: EXPERIENCE FROM A CENTER IN SOUTHERN BRAZIL

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Introduction. D-MELD score, the product of donor liver age and MELD score, was a good predictor of survival after liver transplantation in previous studies. The predictor value of D-MELD on mortality after liver retransplantation (RT) has not been studied. **Objectives.** To assess the predictive value of D-MELD on mortality after liver RT in a tertiary hospital in Porto Alegre, southern Brazil. **Material and methods.** We included patients undergoing RT from August 1997 to August 2011 by the Liver Transplantation Group. Recipient variables,

MELD score, donor age, recipient survival and D-MELD score were analyzed. A descriptive analysis of variables was made and survival analysis using Kaplan-Meier method. The relationship between survival after RT and donor age, MELD and D-MELD were evaluated by Cox regression. **Results.** Forty patients underwent 42 RT, 5% of all liver transplants. Two patients underwent a second regraft. The mean recipient age was 48.8 years, 69% were male and 83.3% had white skin color. The median MELD score was 27 and mean donor age was 37.2 years. The mean follow-up was 2.8 years. There were 27 deaths (67.5%), septic shock being the most common cause. There was no statistically significant relationship between recipient survival and donor age, MELD or D-MELD scores. In the subgroup of patients with D-MELD > 1,600, the score was not a predictor of mortality. **Conclusion.** D-MELD was not a good predictor of mortality after RT at our center. Numerous variables related to recipient, donor, surgery and intensive care may obscure the predictive value of D-MELD.

ANALYSIS OF THE PREDICTOR VALUE OF D-MELD ON MORTALITY AFTER LIVER TRANSPLANTATION: EXPERIENCE FROM A CENTER IN SOUTHERN BRAZIL

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Introduction. D-MELD score, the product of donor liver age and MELD score has been proposed as a useful tool for assessing the prognosis of patients undergoing liver transplantation (LT). **Objectives.** To evaluate the predictive value of D-MELD on mortality in a population undergoing LT in Santa Casa de Misericordia de Porto Alegre, Brazil. **Material and methods.** We retrospectively included patients undergoing LT between July 2006 and June 2011 by the Liver Transplantation Group. Recipient and donor variables were studied. A descriptive analysis of variables and survival analysis using Kaplan-Meier method were made. Logistic regression, Cox regression and ROC curve were used to describe the relationship between risk of death and D-MELD, the latter evaluated as continuously and categorized variable (0-800, 800-1,200 and ≥ 1,200). **Results.** We included 233 patients. The mean recipient age was 54.3 years and 67.8% were male. The most common indication for LT was hepatocellular carcinoma (58.4%). The mean MELD score was 16.3 and mean donor age of was 44.9 years. The median D-MELD score was 650 (range 84-2,701). The mean follow-up was 47.1 months. Survival rates at 1, 3 and 5 years after LT were 79%, 70% and 60%, respectively. Logistic regression and Cox regression showed no statistically significant relationship between mortality and D-MELD, as continuous and categorized variable. The AUC was 0.53 for continuously evaluated and 0.54 for categorized D-MELD. **Conclusion.** We found no statistically significant relationship between D-MELD and mortality in our center. Understanding interactions between donor and recipient remains important to get better results.

HEPATIC SUBCAPSULAR HEMATOMA FOR INVASIVE FASCIOLIASIS

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Purpose. To report a case series of spontaneous hepatic subcapsular hematoma due to invasive fascioliasis. **Material and methods.** Retrospective review of five patients's records with no history of recent trauma, entering emergency with abdominal pain of sudden onset and severe anemia, hepatic subcapsular hematoma and marked eosinophilia. **Results.** One female (15y/o) and 04 males (27, 31, 48 and 55 y/o). Four cases progressed with hypotension and severe acute anemia [mean Hb: 6.1 g% (4.2-8.9)]. Two come from high prevalence areas of hepatocellular carcinoma and three come from farming regions. Ultrasonography revealed an irregular tumor with suspicion of neoplastic disease. CT scan showed three giant hepatic subcapsular hematoma in right lobe, one of moderate size in segments II-III and the last case in segment I. In all cases also appreciated an ill-defined image with scarce and irregular uptake of contrast into the adjacent parenchyma, simulating a solid liver tumor complicated with spontaneous bleeding. Hematological studies evidenced leukocytosis and marked eosinophilia [mean 4,120/mL (2,340-5,120)]. LFT and serological markers of viral, parasitological or tumor were negatives. Arc 2 was positive in 03 cases and indeterminate in one. A Western-blot test confirmed the diagnosis in all cases. Treatment with 02 doses of triclabendazole (10 mg/kg). The outcome was favorable with complete remission of symptoms and gradual normalization of eosinophilia and progressive resolution of hematomas. **Conclusions.** Spontaneous hepatic subcapsular hematoma is a rare entity. The hepatic fascioliasis should be considered as part of differential diagnosis, especially in cases associated with eosinophilia, in order to make the approach and treatment possible, and avoid unnecessary surgery.

POLYCYTHEMIA SECONDARY TO FOCAL NODULAR HYPERPLASIA. A CASE REPORT

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Purpose. To report a case of polycythemia secondary to FNH that resolves after surgical resection. **Material and methods.** Reviewed the child medical record misdiagnosed by polycythemia vera who is discovered incidentally a solid liver tumor. Surgical treatment and histological study supports variant telangiectatic of focal nodular hyperplasia. **Results.** A 11 y/o female, asymptomatic, with adequate school and physical performance, was incidentally discovered polycythemia (Hb: 23 g%). Hematology reappraisal evidenced high dosage of erythropoietin, so imaging studies are performed and solid-looking liver tumor is discovered. Angio MS-CT, shows 8 x 7 cm tumor, with early and irregular contrast enhancement and slow washout with hypodense center suggestive of necrosis vs. eschar, with well-defined feeding artery from right hepatic artery. Sulfur colloid liver scintigraphy shows enhancement of the radiopharmaceutical in right liver posterior views. MRI shows solid lesion with irregular contrast enhancement in arterial phase with central hypointense on T1 and hyperintense on T2, and contrast captured in late stages, which is characterized as vascular fibrosis. It's considered that polycythemia is secondary to liver tumor producing erythropoietin, for which surgical management is performed: right posterior lateral sectionectomy is performed. Outcome is normal levels of erythropoietin and hemoglobin (12 g/dL), returning to their schooling. Histological examination showed features of focal nodular hyperplasia with extensive areas of vascular lakes (which explains the radiological irregular behavior of the lesion), which characterize the telangiectatic variant. **Conclusion.** FNH may be a rare cause of secondary polycythemia (most frequently associated with neoplastic tumors) and resolved definitively with surgical management.

AD-MMP8 ADMINISTRATION IN SKELETAL MUSCLE REDUCES PROFIBROGENIC GENE EXPRESSION IN A MODEL OF EXPERIMENTAL LIVER CIRRHOSIS

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Purpose. The purpose of this work was to demonstrate experimental fibrosis reversion through MMP8 production in skeletal muscle after muscularly administering AdMMP8 in rats intoxicated with thioacetamide (TAA). **Material and methods.** Experimental liver fibrosis was induced in male Wistar rats by TTA administration for 7 weeks. Four groups of rats (n = 15) were included: control (without fibrosis), TAA induced-cirrhosis (TAA), TAA + AdGFP (vector with an irrelevant gene) and TAA + AdMMP8 (vector with a therapeutic gene). At the beginning of the fifth week of TAA intoxication, vectors were administered in soleum muscle. Sub-groups of rats (n = 5) were sacrificed at the end of week one, two and three after vector administration. We measured the percentage of fibrosis, liver function tests, gene expression of MMP8, proinflammatory genes (IL-1 beta, TNF alpha), profibrogenic genes (collagen I and TGF beta) and antifibrogenic genes (MMP1 and MMP9). **Results.** Group treatment with the vector AdMMP8 during the 3 weeks, maintaining MMP8 protein expression, decreases fibrosis up to 48%, does not increase the expression of proinflammatory genes, profibrogenic gene expression decreases ($p<0.05$), increases the expression of antifibrogenic genes ($p < 0.05$) and reduced liver function tests was not statistically significant. **Conclusions.** Therapeutic protein (MMP8) was expressed 21 days of treatment, the vector did not generate inflammation in the liver of animals with fibrosis, treated animals show a decrease of profibrogenic gene expression, showing prevention of liver fibrosis. With these results we can start working with the model of reversal of liver fibrosis in the experimental model.

COINFECTED HIV-HCV PATIENTS: SPONTANEOUS CLEARANCE OF HCV AFTER LIVER TRANSPLANT

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Purpose. To show whether HIV-HCV coinfected liver transplant patients present spontaneous clearance of HCV. **Material and methods.** Prospective and descriptive study between 1st January 2001 and 31st December 2011 of HIV-HCV coinfected liver transplant patients. **Results.** Eight out of nine HIV infected liver transplant patients (88.8%) were HCV coinfected; only 1 (12.5%) developed HCV viral spontaneous clearance. A 38-year-old male patient, ex-PVDA, HIV+ stage C (antiretroviral treatment with Enfuvirtida, Zidovudina and Raltegravir) and hepatic cirrhosis secondary to HCV genotype 1 with no response to INF and Ribavirin. Liver transplant is performed: MELD 30, HIV copies < 50 UI/mL, CD4+ 486, HCV copies 2,564 UI/mL. One month after the transplant and being treated with cyclosporine A (CsA), micophenolate mofetil (MMF) and prednisone as immunosuppressive therapy, he develops acute cellular rejection; metilprednisolone is added and cyclosporine is changed to tacrolimus. Progression of liver disease is appreciated and complementary tests show it is secondary to HCV recurrence (56.5×10^5 copies UI/mL, hepatic biopsy). At this moment, HIV-RNA viral load is no detectable and CD4+ is 238. The patient initiates treatment with αINF and Ribavirin, together with eritropoyetin and GCEF; due to side effects and interactions with antiretrovirals, the antivirals are suspended. Spontaneously and progressively HCV-RNA viral load decreases until becomes negative 5 months after liver transplant. The patient needed re-transplant but HCV-RNA viral load continues being negative after 15 months. **Conclusions.** Most HIV liver transplant patients are coinfected with HCV. The spontaneous clearance of HCV in HIV-HCV coinfected liver transplant patients is possible and it persists even after retransplant.

TREATMENT OF LYMPHOPROLIFERATIVE DISEASES IN LIVER TRANSPLANT PATIENTS: RESPONSE TO RITUXIMAB®

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Purpose. To determine the incidence and treatment of lymphoproliferative diseases in liver transplant patients (Post-Transplant Lymphoproliferative Disorder -PTLD-). **Material and methods.** Prospective descriptive study of liver transplant patients diagnosed with lymphoproliferative disorder (PTLD). **Results.** Only 1 out of 220 liver transplant patients (0.45%) developed PTLD. A 64-year-old male patient with hepatocellular carcinoma and alcoholic liver cirrhosis with positive serology for CMV and negative for EBV, hypertension and ischemic heart disease (stent in anterior descendent coronary artery) who is liver transplanted (donor: EBV +). As induction immunosuppressive therapy tacrolimus, mycophenolate mofetil and prednisone. Nine months after transplant, he suffers from a bowel obstruction episode and is urgently operated: retroperitoneal mass infiltrating right colon and bladder (right hemicolectomy and Brooke ending ileostomy). Anatomopathological examination of the resected: large cell inmunoblastic lynphoma. Other tests performed: mass in mesograstrium affecting retroperitoneum, several metabolically positive hepatic nodes, cell B lymphoma, EBV-PCR 1,800 copies UI/mL, elevated LDH levels, β_2-microglobulin and ESR. Change in immunosuppressive therapy: anticalceurinic drugs are withdrawn, mycophenolate mofetil is maintained and two new drugs are added: sirolimus (mTor) at low range doses and anti-CD20 monoclonal antibodies (Rituximab®, 4 doses). The patient undergoes clinical and analytic improvement, sustained negative EBV-PCR and absence of active images in Pet-TC; therefore, complete and maintained response of large cell inmunoblastic lymphoma (type B) to the immunosuppressive therapy administered, even one year after. **Conclusions.** The incidence of PTLD is low. After one year of follow-up, complete response is obtained with Rituximab®.

EFICCACY OF BEZAFRIBATE COMBINED WITH URSODEOXICOLIC ACID IN PATIENTS WITH PRIMARY BILIARY CIRRHOSIS WITH SUBOPTIMAL RESPONSE TO TREATMENT

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Purpose. To evaluate both the safety and efficacy of adding bezafibrate to the treatment in patients with primary biliary cirrhosis (PBC) and partial response to Ursodeoxicholic acid (UDCA) in optimal dose (13-15 mg/kg/day). **Material and**

methods. 48 patients with partial response to UDCA (persistent elevation of serum alkaline phosphatase –AP– > 2 times the upper limit of normal after at least 6 months of therapy with UDCA) to whom bezafibrate (400 mg/day) was added. 18 asymptomatic patients completed 4 years of therapy and a new liver biopsy was performed. Then, liver biochemistries and clinical evaluations were performed every 3 months during the study period. Ludwig criteria and modified Ishak score were used to analyze the stage and to evaluate inflammatory activity, respectively. Statistical analysis. Wilcoxon signed-ranks test. **Results.** 18 patients had been treated with UDCA for 8-166 months (mean 40 m) before bezafibrate was added. Addition of bezafibrate was associated with normalization of AP levels in all patients and significant reductions in the levels of ALT, gamma-glutamyl-transpeptidase, and cholesterol when compared to baseline values. No adverse effects were observed and all patients remained asymptomatic. Liver biopsies performed before bezafibrate was added showed that 10 patients had stage I-II while 8 had stage III-IV. The second biopsy after 4 years showed decreased in 1 or more stage in 8 (44.4%), unchanged in 2 (11.2%) and progression in 8 (44.4%). None of the patients with stage I-II progressed to cirrhosis. Florid bile duct lesions observed at initial biopsy in 9/18 disappeared in 6/9 (66.07%). There was decreased inflammation in 8/18 (44.4%), unchanged in 5/18 (27.8%) and increased in 5/18 (27.8%). In the 10/18 (55.5%) cases that did not increase the histological stage, a strong relationship with inflammatory activity improvement was observed. **Conclusion.** Combined therapy with bezafibrate and UDCA improves the biochemical profile of PBC patients who respond only partially to UDCA, even in those with more advanced stages. Decreased inflammatory activity was associated with the improvement of histological stage, probably attributed to the additional anti-inflammatory effect of bezafibrate. Therefore, combined therapy may be an effective alternative treatment for PBC patients who are refractory to UDCA.

FACTORS PREDICTING IN-HOSPITAL MORTALITY BEFORE TRANSPLANTATION OF ONE-HUNDRED PATIENTS WITH FULMINANT HEPATIC FAILURE

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Introduction. Despite the improvements in intensive care, patients diagnosed with fulminant hepatic failure (FHF) presents high mortality rates during the wait for liver transplantation (LT). The search for factors that indicates poor prognosis could help to optimize patients on the waiting list for the urgent LT. We aimed to evaluate prognostic factors for in-hospital mortality of FHF patients referred to LT. **Material and methods.** We retrospectively studied 100 adult patients with FHF referred to urgent transplantation at our institution from February 2002 to June 2011. Indication for LT was determined according to the O'Grady criteria. We analyzed age, sex, etiology, jaundice-to-encephalopathy and prioritization-to-LT time intervals, grade of encephalopathy, INR, Factor V, bilirubin, creatinine, AST, ALT, lactate and the Model for End-Stage Liver Disease (MELD). All data were collected at the time of prioritization to LT. The outcome end point was LT or in-hospital mortality before LT. **Results.** Seventy-eight (78%) patients were female and the mean age was 35.5 ± 14.7 years. The etiologies were virus in 17% of cases, drug-induced in 29%, autoimmune in 13%, cryptogenic in 34% and other in 7%. The prioritization-to-LT time interval was 1.5 days (0 to 9). The mortality rate of patients waiting for LT was 31%. All survivors (31%) were submitted to LT. At prioritization, non-survivors showed a higher grade of encephalopathy [4 (1 to 4) *vs.* 3 (1 to 4)], increased MELD (44 ± 8 *vs.* 38 ± 8), increased lactate (78.4 ± 48.3 *vs.* 41.8 ± 30.6 mg/dL) and increased creatinine (2.60 ± 2.34 *vs.* 1.55 ± 1.54 mg/dL) compared to the patients submitted to LT ($p < 0.05$). **Conclusion.** At the time of prioritization to LT, FHF patients with a poor systemic condition, i.e., patients with encephalopathy grades 3 or 4, renal impairment, raised MELD scores and high serum lactate levels, have higher risk of in-hospital mortality during the wait for LT. This may suggest an effort to develop early indicators of LT for these patients.

SWINE MODEL OF LIVER AUTOTRANSPLANTATION WITHOUT VENOUS BYPASS

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Liver transplantation in swine has improved surgical technique education and research development. Most surgical techniques are conventional liver transplantation using 1 donor and 1 recipient swine. Aiming to improve the technical trainning of liver tranplantation surgeons, minimizing the number of animals used and the research cost, we discribe an experimental model of liver autotransplantation in swine without venous bypass. **Material and methods.** At the Gastroenteroly Departament of Sao Paulo University os School Medicine, we start with a "J" incision. The dissection of the hepatic hilar structures obey the steps of human conventional liver transplantation. Supraceliac aorta is dissected behind the left diaphragmatic crus. Conventional total hepatectomy is performed after supraceliac aorta clamping. The clamping sequence is: supraceliac aorta, portal, infrahepatic and suprahepatic inferior vena cava (IVC). The auto implant is peformed by suprahepatic, infrahepatic IVC and portal end-to-end running anastomosis, using polypropylene 4.0, 5.0 and 6.0, respectively. Then, the supraceliac aorta clamp is removed and the liver revascularized. Arterial anastomosis is performed using polypropylene 7.0 and, at last, biliary anastomosis using polypropylene 6.0. **Results.** Surgery is performed in an average time of 237 minutes (min). The average time of hepatectomy is 104.6 min. Suprahepatic inferior vena cava (IVC), infrahepatic IVC and portal anastomosis are performed in an average time of 20 min, 7.33 min and 14 min, respectively. Arterial and billiary anastomosis are done in an average time of 14,66 min and 18 min, respectively. The urine output average volume is 2,6 mL/kg/h. The bleeding average volume is 367 mL. **Conclusion.** The liver autotransplantation in swine without venous bypass is a feasible procedure for surgeons practice. It is also a less expensive model, excellent as an experimental model for research.

SURVIVAL AFTER ORTHOTOPIC LIVER RE-TRANSPLANTATION

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Orthotopic liver re-transplantation (re-OLT) is the therapeutic option for many hepatic graft failures. Survival after re-OLT usually is poorer than after primary liver transplantation. Given that there is an organ shortage, it is essential to optimize use of this scarce resource. **Propuse.**

Compare survival between primary liver transplantation and liver re-transplantation. **Material and methods.** A total of 2.666 liver transplants performed at different centers (State of São Paulo, Brazil) were analyzed from July 2006 to February 2012. Kaplan-Meier curves were used to analyze patient survival data with log-rank test analysis for significance. Survival was expressed in months (mean plus standard deviation). **Results.** Of 2,552 primary orthotopic liver transplantations, 114 retransplantations were required. Patient survival of transplantation was 45.6 ± 0.7 months, and survival of re-transplantation was 32.54 ± 3.2 months (< 0,001). **Conclusion.** Similar to other series, re-OLT was associated with poorer survival after liver transplantation.

IMPACT OF DONOR AGE ON SURVIVAL AFTER LIVER TRANSPLANTATION

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The discrepancy between the numbers of donor livers and recipients has become a significant problem. Mortality on waiting list remains high almost universally. A strategy to overcome this problem is use donors with increased risk of graft failure (extended criteria donors). Some donor-related factors, including donor age, are supposed to decrease patient and graft survival. On the other hand, donors with advanced age are a possible source to expand the pool of donors. **Purpose.** To analyze the effect of donor age on survival after liver transplantation. **Material and methods.** A total of 2.666 liver transplants performed at different centers (State of São Paulo, Brazil) were analyzed from July 2006 to February 2012. Kaplan-Meier curves were used to analyze patient survival data with log-rank test analysis for significance. Survival was expressed in months (mean plus standard deviation). We stratified the entire cohort in 3 groups according to donor age: < 40 years (group 1); 40-59 years (group 2); ≥ 60 years (group 3). **Results.** Donors age range: 2-82 years. Mean donor age: 40.9 ± 15.8 years. Mean patient survival: group 1: 45.3 ± 0.97 months; group 2: 45.0 ± 0.93 months; group 3: 43.4 ± 2.0 months (p = 0.789). **Conclusion.** In this cohort, donor age did not affect patient survival. Acceptance of liver grafts from older donors is a possible alternative to expand the pool of donors.

IMPACT OF D-MELD ON SURVIVAL AFTER LIVER TRANSPLANTATION

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Donor and recipient factors influence the probability of survival after liver transplantation. Donor age, donation after cardiac death, split liver donors, graft steatosis, serum sodium and days at intensive care unit are known factors possibly implicated on survival after liver transplantation. MELD score has been used to estimate mortality on waiting-list for liver transplantation and has been used as a tool for prioritize sickest patients for transplantation. Post transplant patient survival depends on both donor quality and preoperative medical condition. D-MELD, the product of donor age and preoperative MELD, has been proposed as a strategy for matching donors and recipients avoiding transplants with inferior outcome. D-MELD scores above 1.600 have been associated with poorer outcomes. **Purpose.** Analyze the effect of D-MELD on survival after liver transplantation. **Material and methods.** A total of 2.666 liver transplants performed at different centers (State of São Paulo, Brazil) were analyzed from July 2006 to February 2012. Kaplan-Meier curves were used to analyze patient and graft survival data with log-rank test analysis for significance. We used a D-MELD score of 1.700 as cut-off. Survival was expressed in months (mean plus standard deviation). **Results**: A D-MELD ≥ 1.700 was found in 606 liver transplants (22.7%). Mean patient survival in D-MELD ≥ 1.700 group was 36.7 ± 1.4 months against 47.4 ± 0.7 in D-MELD < 1.700 group (p < 0.001). Graft survival was poorer in D-MELD ≥ 1.700 group too. Mean graft survival in D-MELD ≥ 1.700 group was 35.4 ± 1.4 months against 43.9% ± 0.7 in D-MELD < 1.700 group (p < 0.001). **Conclusion.** D-MELD is a very simple tool that can assist physicians in making organ acceptance decisions. Applying D-MELD to liver allocation ca eliminate many donor/recipient matches associated with inferior outcome.

FACTORES ASOCIADOS A MORTALIDAD EN PACIENTES CON CARCINOMA HEPATOCELULAR

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Introducción. La incidencia de HCC se ha elevado mundialmente, es la quinta neoplasia más común y la tercera causa de muerte asociada a cáncer y constituye una causa importante de mortalidad en cirróticos (CI). **Objetivo.** Identificar los factores asociados con mortalidad en pacientes con HCC. **Material y métodos.** Estudio de casos consecutivos con revisión retrospectiva de historias médicas de pacientes con diagnóstico de HCC valorados en consultas de Hepatología de dos centros asistenciales de Caracas, entre el 1 de Agosto 1997 y el 27 de mayo 2011. Se evaluaron factores clínicos, epidemiológicos y tumorales asociados a mortalidad en pacientes con HCC. Para el análisis estadístico se utilizó el test de Mann-Witney para variables no paramétricas, test de chi cuadrado para variables paramétricas y curvas de Kaplan Meier para el análisis de mortalidad. Se realizó un análisis multivariado de regresión logística. Se tomó una p < 0,05 como estadísticamente significativa. **Resultados.** Se evaluaron 139 pacientes con diagnóstico de HCC, 23 excluidos por información insuficiente; se incluyeron 116 pacientes. Los pacientes se siguieron por una media de 10,04 ± 2,25 meses. La tasa de mortalidad a los seis meses fue de 31%. No hubo diferencias significativas asociadas a mortalidad en relación con edad, sexo, número de lesiones o tamaño del tumor. La mortalidad fue significativamente mayor (p = 0,002) en pacientes con estadio D (88,8%), seguido de estadio C (52%), estadio B (33,33%) y estadio A (14,28%). Los niveles de alfafetoproteína (p = 0,029), AST (p = 0,033) y ALT (p = 0,04) estuvieron más elevados en pacientes que fallecieron en el seguimiento. La mortalidad fue mayor en pacientes cirróticos que en no cirróticos (86,88 *vs.* 40%, p = 0,029) y en pacientes con tumores con patrón vascular típico (86,79% *vs.* 55,55%, p = 0,044). Asimismo, los pacientes con consumo de alcohol tuvieron una mayor mortalidad (p = 0,046). Las curvas de supervivencia (Kaplan Meier) identificó que niveles de alfafetoproteínas > 20 μg/L y bilirrubina > 1,5 mg/dL se asociaron significativamente con mortalidad a seis meses (p < 0,05). En el análisis multivariado el estadio BCLC (Barcelona Clinic Liver Cancer) y la presencia de invasión vascular fueron predictores independientes de mortalidad a los seis meses (p < 0,05). **Conclusión.** La clasificación de BCLC es un excelente sistema pronóstico en pacientes con carcinoma hepatocelular además de permitir el abordaje terapéutico de estos pacientes, asimismo la presencia de invasión vascular predice el pronóstico de los pacientes con hepatocarcinoma a mediano plazo.

COMPLICACIONES EN EL POSTOPERATORIO INMEDIATO DEL TRASPLANTE HEPÁTICO. EXPERIENCIA EN UNA UNIDAD DE CUIDADOS INTENSIVOS EN LOS ÚLTIMOS OCHO AÑOS

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Introducción. El curso postoperatorio inmediato del trasplante hepático (TxH) está determinado por diversos factores: estado preoperatorio del receptor, complicaciones intraoperatorias, función inicial del injerto hepático y complicaciones infecciosas, respiratorias, neurológicas y hemodinámicas. **Objetivo.** Valorar las complicaciones en el postoperatorio inmediato del trasplante hepático en una Unidad de Cuidados Intensivos (UCI). **Material y métodos.** Estudio descriptivo (ocho años) en adultos que ingresan en UCI tras recibir TxH. El manejo fue según la vía clínica del TxH. Variables analizadas: tipo de injerto, patología de base, gravedad en UCI, complicaciones en UCI (hemodinámicas, respiratorias, infecciosas, hepáticas, hematológicas, metabólico-nutricionales, renales), estancia y mortalidad. Análisis estadístico con SPSSv11. **Resultados.** Durante 2004-2011 ingresaron 530 TxH. Tipo de injerto: muerte encefálica 432 (81,51%); injerto parcial split 25 (4,72%); asistolia 53 (10%); donante vivo 12 (2,26%) y dominó ocho (1,51%). APACHE II: 9,88 ± 4,93 y SAPS II: 25,39 ± 10,63. Tiempo medio de ventilación mecánica 11,92 ± 49 h y tiempo medio de extubación 13,25 ± 8,21 h. Las complicaciones más importantes fueron: trombopenia (100%), hiperglucemia con necesidad de insulina (90%), disfunción renal (60%). La estancia media en UCI fue 4,2 ± 8 días (mediana cuatro días, rango 2-80 días). La mortalidad en UCI fue 5,47%. Los pacientes que fallecieron presentaron mayor edad, nivel de gravedad al ingreso y presencia de complicaciones graves (Shock hipovolémico por hemoperitoneo masivo 51,72%, coagulopatía severa 100%; fracaso renal anúrico con necesidad de técnica de depuración extrarrenal continuo 89,65%; disfunción del injerto 58,62%; episodio de rechazo agudo 20,69%, encefalopatía grave 20,69%, polineuropatía del paciente crítico 20,69%, síndrome de distrés respiratorio agudo 55,17%, arritmias cardiacas graves 27,58%, complicaciones quirúrgicas 14%, shock séptico 44,83%, neumonía asociada a ventilación mecánica 37,93%, sepsis grave por catéter 27,59%, peritonitis bacteriana 6,89% y mucormicosis cutánea invasiva 10,34%). Todos los pacientes desarrollaron fracaso multiorgánico irreversible. Este grupo de pacientes presentaron mayor estancia en UCI (13 ± 14 días). **Conclusiones.** 1. El trasplante hepático presenta una estancia breve en UCI en el postoperatorio inmediato. 2. La frecuencia de complicaciones quirúrgicas es baja. 3. La principal causa de fallecimiento es el fallo multiorgánico secundario a shock séptico. 4. La disfunción del injerto implica mayor grado de complicaciones hemorrágicas con necesidad de revisión quirúrgica.

TRASPLANTE HEPÁTICO EN SÍNDROME HEPATOPULMONAR: RESULTADOS DE UN CENTRO

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Introducción. El síndrome hepatopulmonar (SHP) se caracteriza por disfunción hepática o hipertensión portal, hipoxemia arterial y dilataciones vasculares intrapulmonares, anomalías potencialmente reversibles postrasplante hepático (TH). **Objetivo.** Evaluar las características clínico-epidemiológicas de pacientes con SHP sometidos a TH y su evolución postoperatoria. **Material y método.** Revisión retrospectiva de historias clínicas de pacientes > 14 años con diagnóstico SHP, trasplantados de hígado, durante 2000-2011. **Resultados.** Se identificaron diez casos (10%) de SHP. La relación hombre:mujer fue 1:1, y la edad promedio de 38.9 años (15-61). La etiología de la cirrosis fue hepatitis autoinmune en tres casos (30%), esteatohepatitis no alcohólica dos casos (20%), alcohólica en dos casos (20%), un caso de cirrosis criptogénica (10%) y un caso de enfermedad por depósitos de ésteres de colesterol (10%). Hubo hipertensión portal clínicamente significativa, cuya manifestación principal de enfermedad fue sangrado variceal (siete pacientes) y plaquetopenia (leve un caso, moderada cinco casos y severa dos casos). El estatus funcional hepático fue Child Pugh A un caso (10%), B seis casos (60%) y C tres casos (30%). El MELD promedio fue 18.6 (12-26). La P_aO_2 promedio previa al trasplante fue 52.2 mmHg (23-75), S_aO_2 83.9% (48-93) y la $P_{A\text{-}a}O_2$ 90 mmHg (58-134). En todos los casos el ecocardiograma con test de burbuja fue positivo y la gammagrafía con macroagregados de albúmina con captación cerebral del contraste en promedio 38% (7-77). El SHP fue moderado en cuatro casos (40%), severo en tres casos (30%) y muy severo en tres casos (30%). El tiempo promedio de seguimiento fue de 36.7 meses (5-89) y la mortalidad de 10% (un paciente con SHP muy severo). La estancia promedio en la Unidad de Cuidados Intensivos fue de 13 días (5-34), la duración de ventilación mecánica fue de diez días (1-34) y la necesidad de algún tipo de soporte oxigenatorio de 13.7 días (3-40). La principal complicación respiratoria fue neumonía en dos casos (20%). La estancia hospitalaria total fue en promedio 23.6 días (9-83). La P_aO_2 a siete días postrasplante promedio fue de 54 mmHg (45-62) y a 30 días postrasplante de 89 mmHg (81.4-101). **Conclusión.** El SHP es una complicación frecuente en cirróticos candidatos a TH, cuya causa es desconocida, casi siempre asociada a otras manifestaciones de hipertensión portal. El TH es una medida eficaz en su tratamiento, con una morbimortalidad no superior a la población de trasplantados hepáticos sin esta complicación.

RECONSTRUÇÃO DE VARIAÇÃO ARTERIA HEPATICA DIREITA USANDO UMA TECNICA CARREL PATCH-PERMITE ORIENTAÇÃO RETA NO TRANSPLANTE DE FIGADO

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Introdução. Variante anatomia da artéria hepática é comum, com incidência relatada de 20-50%. No transplante de fígado, de volta tabela de reconstrução é muitas vezes necessário para uma mais fácil e rápida anastomose arterial e para este fim, o uso de adesivos arteriais tem sido demonstrado estar relacionada com menor incidência de complicações. No entanto, quando uma variação da artéria hepática direita (RHAV) a partir da artéria mesentérica superior (SMA) está presente, a reconstrução ocasionalmente produz problemas de torção e de fluxo Desfazer edições. **Materiales e metodos.** Nós desenvolvemos uma alternativa cirúrgica para reconstrução RHAV usando um Carrel-patch da SMA anastomosando com o stumpto artéria esplênica para permitir a orientação vertical e melhorar o fluxo sanguíneo. **Resultados.** Entre os 120 transplantes de fígado, 4 casos consecutivos de RHAV foram reconstruídos usando esta técnica. Todos apresentavam bom fluxo e permeabilidade no período. **Con-**

clusão. A reconstrução proposto mostrou ser o melhor quando comparado com outras opções.

CHOLESTASIS AND CHRONIC AUTOIMMUNE DISEASES

PROGRESIVE FAMILIAL CHOLESTASIS TYPE 3 (PFIC3). FAVORABLE RESPONSE TO URSODEOXICOLIC ACID (UDCA). EVOLUTION OF MORE THAN 8 YEARS

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Progressive familiar intrehepatic cholestasis is a group of rare hereditary diseases as a result of mutations in the canalicular transport systems. The PFIC3 is a consequence of a mutation in the ABCB4 gene with a dysfunction of a phosphatidylcholine flipasa (MDR3); as a result of the absence of secretion of phospholipids, maintaining the release of bile acids and generating damage on the membrane of the cholangiocyte thegamaglutamiltranspeptidase (Ggt) rise. **Aim.** To present a PFIC3 case with a clinical, biochemical and histological improvement after treatment with UDCA. Case: male patient, 23 years old with severe cholestasis diagnosed as PFIC3 by genetic analysis (2 mutations in the gene MDR3, ABCB4), both in heterozygosis and absence of canalicular MDR3 by immunohistochemical staining. The index case was a brother who died at 17 years, by upper gastrointestinal bleeding (esophageal varices) and cirrhosis with severe cholestasis in the liver biopsy (BX). After 56 months of treatment with UDCA (15 mg/kg/d) the patient evolves with disappearance of the cholestasis with an improvement of liver fibrosis in consecutive biopsies. **Discussion.** The PFIC3 is a progressive disease of children and youth. The optimal strategy for the treatment has not been established. Liver transplant is an option. Some studies showed that using UDCA in children may improve the histology. The mechanism of action has not been clarified. In the PFIC3 with partial defect of the MDR3 with a residual concentration of phospholipids in the light of cholaniocytes, UDCA could generate an improvement associated with an early onset of treatment.

CLINICAL FEATURES AND EPIDEMIOLOGY OF PRIMARY BILIARY CIRRHOSIS IN URUGUAY

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Purpose. The Primary Biliary Cirrhosis (PBC), is a chronic hepatopathy, cholestatic autoimmune, produced by the inflammation and destruction of the interlobular bile ducts. It's more frequent among female patients (10/1), during the fifth decade of life and 50 out of 60% of the patients are asymptomatic to the diagnostic. The objective was to describe the clinical and epidemiologic characteristics of patients with PBC in Uruguay. **Material and methods.** It was a descriptive study of an open cohort, in where all the diagnosed patients with PBC were included, treated between January 2002 to September 2011. The diagnosis was based on the cholestasis. AMA o (AMA2) or positive ANA (anticentromere patron) and compatible biopsy. There were recorded, sex, age, symptoms, related illnesses, laboratory results, images and histology at the moment of the diagnosis. **Results.** 81 patients were included (94% women), average age 56 years old (31- 79). The 73% (59 /81) were symptomatic, and the pruritus was the most frequent found on 86% (51/59). The asthenia and jaundice were on the 46 (27/59) and 32% (19/59) respectively. The 84% presented positive AMA. 43% of the patients were biopsied (35/81) and the 37 % of them (13/35) cirrhosis was detected. Ascites was noted on the 10% (8/80). On the 43 % of the patients it was detected at least one autoimmune illness associated. The average survival of the studied population was 10, 6 years. (8, 8-12,4: IC95%). **Conclusions.** In this group, the PBC presented an important prevalence on women, a high percentage on symptomatic patients and on a fourth of the analyzed serie it was shown the presence of cirrhosis at the moment of the diagnostic.

DECOMPENSATION SEVERE OF AUTOIMMUNE HEPATITIS BY VIRUS HEPATITIS E INFECTION: CASE REPORT

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Introduction. Viral infections sometimes lead to decompensation of autoimmune liver disease. **Case report.** Female patient, 16 years old, asymptomatic, without history of transfusions, surgeries, alcohol or drug consumption. After a trip, she developed symptoms like asthenia, fever, jaundice, dark urine, and then abdominal pain on right upper quadrant. In our hospital, she was diagnosed with viral hepatitis E infection. At follow-up examinations, they identified persistent elevation of aminotransaminases and prolonged prothrombin time (aprox. 6 month), so the doctors decided to stay in the hospital. Clinical examination showed a no consumptive patient with skin and mucous jaundice, liver palms and hepatomegaly, without evidence of encephalopathy. **Auxiliary tests.** AgVHBs, Anti HBc and Anti HCV: No Reactive. HEV IgM: Reactive. ANA, ASMA, Anti LKM-1 and AMA: Negative. HIV: No Reactive. Serum ceruloplasmin and copper levels, transferrin saturation, ferritin and alpha 1 anti trypsin in normal ranges. Liver biopsy revealed distorted liver parenchyma with the presence of portal fibrous bridges holder, mixed inflammatory infiltrate with predominance of lymphocytes and plasma cells; which crossed the limiting plate. The diagnosis was chronic liver disease, which was associated to viral chronic infection for VHE or secondary to autoimmune hepatitis. However chronic infection for VHE is associated with immunosuppression, a condition not present in the patient. The patient was treated with prednisone and azathioprine autoimmune hepatitis. On the fourth month of starting treatment aminotransaminases and prothrombin time were normal. **Conclusion.** This was the evolution of a case of decompensation severe of autoimmune hepatitis by virus hepatitis E infection.

CLINICAL AND EPIDEMIOLOGICAL FEATURES OF NEONATAL CHOLESTASIS IN HOSPITALIZED PATIENTS. INSTITUTO NACIONAL DE SALUD DEL NIÑO. 2011

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Purpose. To describe the clinical and epidemiological characteristics of neonatal cholestasis in the Instituto Nacional de Salud del Niño, 2011. **Material and methods.** The sample

consisted of 48 infants with a diagnosis of cholestasis. We analyzed the variables sex, age at diagnosis, gestational age and birth weight, perinatal and postnatal history, place of origin, presenting symptoms, clinical examination signs and etiology of cholestasis. After that, we developed a database of SPSS 15 and then, we analyzed the variables. **Results.** There was a predominance of male infants (70.8%), term infants (62.5%) and normal weight (58.3%). The average age was 112.42 days, 29.2% patients were seen within the first 2 months of age. The most common symptoms were jaundice (100%), choluria (70.8%), hipocolia (56.6%) and acholia (12.5%). The different causes of cholestasis were: biliary atresia (29.2%), cytomegalovirus infection (12.5%), thick bile syndrome (6.3%), idiopathic neonatal hepatitis, cyst common bile duct, inborn error of metabolism and progressive familial intrahepatic cholestasis in 4.2%. The diagnosis could not be found in 13 patients (27.1%). **Conclusions.** The clinical and epidemiological data obtained in this study are similar to those reported by different series of neonatal cholestasis.

ANALYSIS OF THE INFLUENCE OF THE *ABCB11* 1331T>C POLYMORPHISM ON FUNCTIONAL INTERACTIONS AT THE BSEP TRANSPORTR PROTEIN ACTIVE SITES AND DRUG-INDUCED LIVER INJURY (DILI)

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Objetives. The BSEP (bile salt export pump) is a membrane transporter, present in hepatocytes, responsible for the elimination of bile salts via the bile canaliculus. To perform its function BSEP requires simultaneous binding of ATP and TAU (taurocholate) substrates. **Purpose.** To analyze the role of the *ABCB11* 1331 T>C polymorphism in the development of DILI induced by ibuprofen and amoxicillin-clavulanate. **Material and methods.** The BSEP amino acid sequence was obtained from www.uniprot.org. Molecular modeling of the functional domain corresponding to the T and C allele sequences was performed using the swiss-model service. The igemdock program was used to calculate docking scores. The *ABCB11* 1331T>C polymorphism was genotyped in 46 DILI patients induced by amoxicillin-clavulanate (n = 39), ibuprofen (n = 6) or amoxicillin (n = 1), using Taqman probes. **Results.** The presence of the C allele (corresponding to an alanine in the protein) modifies the active sites of TAU and ATP, slightly decreasing the binding affinity for these substrates.For the amoxicillin-clavulanate cases the C allele (66% of the patients) promotes the occupation of both the active sites (but not for amoxicillin or clavulanic acid separately). In addition, new binding sites appear that interact with the drug's aromatic ring through Van der Waals forces, which can alter the excretory function of the protein and the retention of cytotoxic compounds in the hepatocyte. In case of ibuprofen the C allele (83% of the patients) only resulted in an altered interaction at the TAU active site, in conjunction with the formation of new drug binding sites. **Conclusions.** Patients carrying the C allele have an increased risk of liver toxicity when exposed to amoxicillin-clavulanate and ibuprofen, due to the occupation of both the TAU and ATP active sites and the ATP active site alone in amoxicillin-clavulanate and ibuprofen case, respectively. New binding sites owing to the C allele, have a higher affinity for aromatic rings present in these drugs. These data suggest that the occupation of TAU and ATP sites together with an increase in the number of drug binding sites, could result in increased exposure of hepatocytes to bile salts (TAU) and the drug, increasing the risk of liver toxicity.

HEPATITIS AUTOINMUNE DE PRESENTACIÓN AGUDA

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Introducción. La hepatitis autoinmune (HAI) es una hepatopatía crónica y progresiva de etiología desconocida, caracterizada por autoanticuerpos e Ig G elevadas. Tiene comportamiento heterogéneo y fluctuante, desde presentación asintomática hasta hepatitis aguda severa y fulminante. **Objetivo.** Analizar características clínicas, de laboratorio, histológicas y evolución de pacientes con HAI de presentación aguda. **Material y métodos.** Se realizó una revisión retrospectiva de pacientes con HAI de presentación aguda en HCUCH y CLC entre 2003 y 2011. Se clasificaron en tres grupos: A) HAI fulminante: protrombina (TP) < 50% asociado a encefalopatía. B. HAI severa: TP < 50% y C) HAI aguda: bilirrubina total (BT) > 10 mg/dL y/o transaminasas mayor a 15 veces el valor normal. Se descartaron otras causas de hepatitis aguda. **Resultados.** Se incluyeron 58 pacientes, siete (12%) en grupo A, 19 (33%) en grupo B y 32 (55%) en grupo C, edad promedio 48 ± 15 años (16-82), sexo femenino siete pacientes (100%) en grupo A, 13 (68%) en grupo B y 27 (84%) en grupo C. BT (mg/dL) fue 22 ± 10 en grupo A, 16 ± 8 en grupo B y 12 ± 9 en grupo C ($p < 0.002$ entre A y C), SGPT (mg/dL) fue 1,795 ± 1,139 en grupo A, 1,236 ± 522 en grupo B y 1,352 ± 590 en grupo C (p NS), TP (%) fue 26 ± 12 en grupo A, 42 ± 9 en grupo B, 71 ± 13 en grupo C ($p < 0.008$). En marcadores de autoinmunidad se encontró ANA (+) en cuatro pacientes (67%) del grupo A, 14 (74%) del grupo B, dos (81%) del grupo C (p NS), ASMA(+) en tres pacientes (50%) del grupo A, siete (41%) del grupo B y 15 (71%) del grupo C (p NS) e Ig G sobre el valor normal en cuatro pacientes (80%) del grupo A, 13 (72%) del grupo B y 19 (76%) del grupo C (p NS). En biopsia se observó hepatitis crónica en seis pacientes (86%) del grupo A, 12 (63%) del grupo B, 27 (84%) del grupo C (p NS), necrosis en siete pacientes (100%) del grupo A, 14 (74%) del grupo B y 14 (44%) del grupo C ($p < 0.006$), fibrosis en dos pacientes (33%) del grupo A, nueve (47%) del grupo B y 25 (78%) del grupo C (p NS). Se trasplantaron cuatro pacientes del grupo A. **Conclusión.** HAI de presentación aguda puede tener evolución catastrófica. Afecta principalmente a mujeres de cualquier edad. Marcadores de autoinmunidad y valor de transaminasas no diferencian distintos tipos de HAI de presentación aguda. El grado de necrosis en biopsia hepática sería factor de mal pronóstico.

HEPATIC TUMORS

HEPATIC EPITHELIOID HEMANGIOENDOTHELIOMA: DIAGNOSTIC AND THERAPEUTIC IMPLICATIONS OF AN INFREQUENT NEOPLASIA: A CASE REPORT

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Purpose. Multifocal hepatic epithelioid hemangioendothelioma is a vascular origin tumor characterized by a low-grade malignancy endothelial proliferation it's a very rare neoplasia. We report the first liver transplantation for this disease in Uruguay, and perform a brief review. **Materials and methods.** Case report and literature review. **Results.** 52 year old woman diagnosed with breast ductal carcinoma (02/2009) mucinous type, stage "Ia", complete oncologic treatment. At 11/2010, in outpatient control showed a slight increase of gamma-glutamyl transpeptidase and phosphatase alkaline. Abdominal CT showed 11 nodular lesions from 12 to 29 mm compatible with multiple liver metastatic lesions. A laparoscopy evidence metastatic liver appearance, directed biopsy was performed. Pathology report. Diffuse and infiltrating proliferation of medium size cells, arranged predominantly in isolation. Individually the cells presents an hyperchromatic eccentric nuclei, and often have intracytoplasmic vacuoles, some of which show red blood cells. Shows scarce stromal tissue predominantly fibrous connective. The cells are intensely and diffusely positive for Vimentin, CD3, CD34 and less intensity for factor VIII markers. Discussed the case in multidisciplinary team is decided to perform a liver transplant. Entered to the waiting list in 28/07/2011, transplanted on 09/02/2012 and discharged 15/02/2012. **Conclusions.** Entity first described in 1982, estimated incidence of primary liver less than 0.1 case/100.000 inhabitants/year. Most frequent in young adults, female and Caucasian. Clinical presentation: mostly asymptomatic, and mimic multiple liver metastatic lesions in CT and US. In this case the treatment is liver transplantation. The prognosis is very favorable with 5 years survivals between 54.5% and 83% in largest series.

INCIDENCE AND RISK FACTORS FOR HEPATOCELLULAR CARCINOMA IN PATIENTS WITH CHRONIC HEPATITIS B IN BELO HORIZONTE (BRAZIL)

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Objectives. This study evaluated the incidence and risk factors for HCC in the last decade in a Reference Center for Viral Hepatitis in Belo Horizonte (Brazil). **Material and methods.** Demographic and clinical data of patients admitted to hospital for treatment of hepatitis B in the last 10 years were analysed. Confirmatory methods of HCC were CT and/or MRI. Alcohol abuse was considered as ingestion of alcoholics over 30 g and 20 g for men and women, respectively, for at least one year. **Results.** 404 patients were eligible for analysis. The incidence of HCC in HBV patients was 5.7% in 10 years. 87.0% patients with HCC were male, 60.9% aged > 50 years, 87.0% were cirrhotic, 66.7% had HBVDNA > 2,000 IU/mL ($8.2 .10^7 \pm 1.9 .10^6$ IU/mL). 65.2% patients were HBeAg negative, 61.9% smokers and 50.0% alcoholics. Risk factors for HCC were age > 50 years (mean 52.4 *vs.* 43.7, $p = 0.001$), alcoholism ($p = 0.006$), smoking ($p = 0.027$) and cirrhosis ($p < 0.001$), but cirrhosis was the only risk factor for HCC in the multivariate analysis (OR = 16.85, 95% CI 4.90-57.87, $p < 0.001$). No association among HBeAg status, higher HBV DNA load and HCC were observed. **Conclusions.** Cirrhosis was the main risk factor to HCC in male patients > 50 years, regardless the HBV DNA load or the status of HBe antigen. This study reiterates the importance of systematic screening of HCC in patients with chronic hepatitis B with these characteristics.

HEPATOCARCINOMA IN CHILDREN: THIRTEEN-YEARS EXPERIENCE OF A PEDIATRIC ONCOLOGY TEAM IN PERU

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Purpose. To describe the epidemiology, treatment and outcome of hepatocarcinoma in children from Peru. **Material and methods.** A retrospective review type cases serie of children less of 18 years old with the diagnosis of hepatocarcinoma treated in our institution (Rebagliati Hospital) from January 1999 to March 2012. Data collected included demographic, clinical radiologic, pathologic, treatment and outcome. **Results.** There were 19 patients with the diagnosis of hepatocarcinoma. Their median age was 8 years old. There were 5 girls and 14 boys (relation 1/3). Procedents of coast 52.6%, mountains 36.8% and forest only 10.5%. The main signs were hepatomegaly, abdominal mass, vomiting, weight loss, anemia and pain. Only 7 patients (37%) received hepatitis B vaccine, 6 patients (31.7%) had chronic hepatitis B of these patients all (100%) did'nt receive hepatits B vaccine. Only one case had metabolic disease: Tirosinemia. The alphafetoprotein median level at diagnosis was 86,940 ng/mL (range from 300 to 349,650). The SIOPEL stages were Pretext 4: 26%, Pretext 3: 58%, Pretext 2: 15% and Pretext I: 0%. Five patients (26.3%) had initial metastases (lung, brain and skin). The histology was epithelial hepatocarcinoma in all cases and 4 (22%) had cirrhosis. Four patients had primary surgery (one patient submitted transplant who had Tirosinemia and three patients had liver resection), three patients after surgery received chemotherapy but only who received chemotherapy with sorafenib is alive. 15 patients had unresectable disease at beginning; of these last patients, 4 received chemotherapy alone (based on SIOPEL protocols), 5 patients received systemic chemotherapy with hepatic intra-arterial doxorubicin; and 6 patients received systemic chemotherapy and sorafenib, after this treatment in eleven patients (73.3%) the tumor decrease and they can submitte to surgery. The 4 patients with cirrhosis all died but only one had Ag HBs positive too. Of 6 patients with AgHB (+) all received lamidovudina during the treatment, 5 died (83.3%) by relapsed or progression of disease but only one is alive of hepatocarcinoma with viral charge negative for hepatitis B. At the moment, there are 6 patients alive without disease and 13 patients died (5 had disease progression, 5 relapsed, 2 post-chemotherapy complication and 1 liver failure). The survival global for 6 survivors is 3.6 years (range from 1 year to 6 years). **Conclusions.** Hepatocarcinoma is a bad prognosis disease. The initial approach and multidisciplinary treatment is very important in improving the outcome. The hepatitis B vaccine decreases the risk of hepatocarcinoma in infants and the prognostic is poor if the patient didn't receive hepatitis B vaccine. The role of sorafenib in children with hepatocarcinoma is still uncertain even the patients with this drug didn't have relapse.

IMPACT OF A SURVEILLANCE PROGRAM OF HEPATOCELLULAR CARCINOMA IN A REFERENCE SERVICE OF LIVER DISEASE IN URUGUAY (12 YEARS OF EXPERIENCE)

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Purpose. Early diagnosis of hepatocelular carcinoma (HCC) permit to establish allegedly curative treatments. The aim of

this study is to evaluate the utility of a surveillance program in our population of cirrhotic patients. **Material and methods.** A descriptive, observational retro-prospective study of the patients with HCC (included or not in surveillance program). The survey was retrospective in 01/01/2000-31/08/2010 and prospective 31/08/2012-31/01/2012. For diagnosis, staging, and treatment were taken Barcelona Clinic Liver Cancer (BCLC) and Milan criteria. The monitoring program was scheduled as recommended by American Association for the Study of Liver Disease. Were analyzed: age, gender, liver disease, etiology, BCLC and Milan staging criteria. **Results.** Of the 75 patients included, 47% were diagnosed under a surveillance program. Of these, 80% were within Milan criteria. Regarding BCLC, 76% were in stage A, 6% B, 6% C, and 12% D. The most common etiology was alcoholic liver disease (ALD) in 40%. In the group not under surveillance program (53% of total) most diagnoses were incidental or presenting symptoms of advanced disease. 90% were outside Milan criteria. According the BCLC, 62% were in stage D, 28% C, 7% B, and 3% A. ALD was also the most common etiology in 80% cases. In 26 patients (35%) were established supposedly curative treatments (of which 77% were transplanted, 23% surgical resection or ablative therapy). Of these, 74% were from de surveillance group, and 2% from not surveillance group. **Conclusions.** Most patients under surveillance were diagnosed in early stages, with the possibility of allegedly curative treatments.

EPIDEMIOLOGICAL ASPECTS OF HEPATOCELLULAR CARCINOMA IN A REFERENCE CENTER OF URUGUAY (12 YEARS EXPERIENCE)

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Purpose. Contribute to the knowledge of aspect related to epidemiology, diagnosis and staging of hepatocellular carcinoma (HCC) in Uruguay according to experience in our center. **Material and methods.** A descriptive, observational retro-prospective study of the patients with HCC was performed. The survey was retrospective in 01/01/2000-31/08/2010 and prospective 31/08/2012-31/01/2012. For diagnosis, staging, and treatment were taken Barcelona Clinic Liver Cancer (BCLC) and Milan criteria. Were analyzed: age, gender, liver disease, etiology, Child-Pugh score (CTP), BCLC and Milan criteria. **Results.** Of 78 patients with HCC, 91% were men. The mean age was 60 years. 96% were cirrhotic. Within non-cirrhotic (4%), 66% were NASH. Within the group of cirrhotic patients, 62% had alcoholic cirrhosis, 52% as only noxa, 10% associated with other (HBV, HCV, and hemochromatosis). Other etiologies: 18% HCV, 7% HBV, 4% hemochromatosis, 3% NASH, autoimmune hepatitis 3% and 3% co-infection HBV / HCV. According to the staging of CPT, 23% were stage A, 43% stage B and 34% stage C. 42% was within Milan criteria, 74% of them as a single lesion < 5 cm in diameter, and 26% with < 3 lesions < 3 cm. 58% who were outside the Milan criteria, most presented with multiple lesions or with diameters > 3 cm, but unusual presentation metastatic or vascular invasion Regarding BCLC staging, 36% were in stage A, 7% stage B, 19% stage C and 38% stage D. **Conclusions.** In our series general epidemiological characteristics were similar to reported in the region. Highlights the difference a higher prevalence of alcoholic liver disease over HCV.

SURVIVAL PROGNOSTIC FACTORS FOR CIRRHOTIC PATIENTS WITH HEPATOCELLULAR CARCINOMA

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Purpose. Hepatocellular carcinoma (HCC) is one of the main causes of death among cirrhotic patients. It is critical to know the factors related to its prognosis. The purpose of this study is to analyze the variables related to survival in a cohort of cirrhotic patients diagnosed with HCC in our centre. **Material and methods.** We retrospectively evaluated a cohort of cirrhotic patients diagnosed with HCC in our centre between 2001 and 2010. Clinical and demographic variables were registered as well as the treatments employed and survival. The tumoral stage was defined employing BCLC staging system. The following strategies were defined as treatments with curative intention: Liver transplantation planified liver resection, and radiofrequencyablation in cases of no more than three tumors, no bigger than 3 cm each. We employed Kaplan-Meier curves and log Rank tests to compare different survivals and Cox regression to identify prognostic factors. **Results.** 158 patients we evaluated, median age 65 year old (60-72), male 69%. The follow up length was 25 ± 20 months. In 68% of the patients any treatment was performed (trans-arterial chemoembolization, alcoholization, radiofrequency ablation, planified liver resection or liver transplantation) and in 45% of them the treatment had a curative intention (curative group). Three year survival in the curative group was 72% *vs.* 51% in the non curative group (Log Rank = 0,012). Variables associated to a reduced survival were a tumoral size > 55 mm, (HR 1,87 IC 95% 1,04-3,4), extrahepatic metastasis (HR 3,2 IC95% 1,2-8) and alpha fetoprotein > 22 UI/mL (HR 0,2 IC 95% 1,2-4,8). BCLC stage A (HR 0,6 IC95% 0,31-0,98) and liver transplantation (HR 0,2 IC95% 0,1-0,9) were associated to a reduced mortality at three years. In multivariate analysis, extrahepatic metastasis and lymphadenopaties were associated to a higher mortality at three years (HR 3,95 and 3,57 respectively). In the curative group liver transplantation was associated to a reduced three years mortality (HR 0,3 IC95% 01-0,7). In the palliative group extrahepatic metastasis and BCLC stage D were associated to a higher mortality in the multivariate analysis (HR 13,1 and 6,2 respectively). **Conclusion.** Extrahepatic metastases and tumoral lymphadenopaties were predictive factors independently related to a reduced survival in HCC patients. In patients whom received treatments with non curative intention, extrahepatic metastases and BCLC stage D were predictive factors related to a reduced survival. In the group who received treatments with curative intention, liver transplantation was the only variable independently related to a higher survival.

CARACTERÍSTICAS CLÍNICO-EPIDEMIOLÓGICAS DEL CARCINOMA HEPATOCELULAR, EN EL DEPARTAMENTO DEL APARATO DIGESTIVO DEL HNERM. Es-SALUD. LIMA, PERÚ

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Introducción. El carcinoma hepatocelular (CHC) es la quinta causa de mortalidad por cáncer en el mundo y en la actuali-

dad constituye un problema de salud pública, las características epidemiológicas varían de acuerdo con cada país o región, por lo que se hace necesario la identificación de estas características en cada población. **Objetivo.** Determinar las características clínico-epidemiológicas de los pacientes con diagnóstico de CHC. **Material y métodos.** Estudio prospectivo longitudinal que incluyó a todos los pacientes con diagnóstico de carcinoma hepatocelular, basado en dos o más estudios radiológicos típicos de una lesión hepática > 2 cm o un estudio radiográfico y nivel de AFP > 200 ng/mL para el caso de pacientes cirróticos y con confirmación histológica para los pacientes sin cirrosis, que ingresaron al Departamento de Aparato Digestivo del HNERM-EsSalud entre el 1 de agosto 2007 y el 31 de febrero 2012. **Resultados.** Se incluyeron 131 pacientes con edad promedio de 63.7 años (16-92). El 50% fueron varones, y 85% tenía cirrosis. La edad promedio de éstos fue de 68,1 años, siendo en los pacientes no cirróticos 38,1 años ($p < 0,001$). La etiología asociada más frecuente fue el virus de hepatitis B con 38%, seguida de etiología no determinada/criptogénica 21% y el virus de hepatitis C 18%. Si se considera la etiología en los pacientes sin cirrosis, 89% fueron relacionados con hepatitis B. Sólo 54% de los pacientes se encontraban en programa de despistaje y únicamente 59% tuvo niveles de alfa fetoproteína > 200 ng/mL. En los pacientes con cirrosis hepática, sólo 13% tenía una clasificación BCLC temprana (A) y sólo 47% de la población recibió algún tratamiento dirigido al manejo del CHC. El 80% de pacientes en estadio temprano de la clasificación BCLC fueron sometidos a alguna terapia con intensión curativa y 20% de éstos lograron un trasplante hepático. **Conclusiones.** El 85% de los pacientes con CHC se desarrollan en el contexto de pacientes cirróticos. La edad promedio fue de 63.7 años y la etiología principal es la asociada con el virus de hepatitis B, principalmente en pacientes no cirróticos. A pesar de que 59% de pacientes se encontraban en programa de despistaje, sólo se pudieron identificar 13% de pacientes en estadios tempranos.

ALCOHOLIC LIVER DISEASE AND FATTY LIVER

SMOKING AND NON ALCOHOLIC FATTY LIVER DISEASE IN A GROUP OF MEXICAN PATIENTS. THE ROLE OF OXIDATIVE STRESS. A PILOT STUDY

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Background and aim. There is evidence suggesting that smokers, even showing a lower body mass index, tend to accumulate visceral fat. Exposure to cigarette smoke causes high oxidative stress and stimulates lipid accumulation in the liver. The aim of this study is to investigate the prevalence and the factors associated with NALFD in a group of heavy smokers. **Material and methods.** We included a cohort of 47 smokers who attended a tobacco cessation unit. Anthropometric and biochemical variables were measured in all patients through the treatment. Smokers were included in the tobacco cessation treatment during 10 weeks, cessation was set on week three. Blood samples were taken on week 2, week 4, and week 10. **Results.** We found a proportion of 76% of NAFLD in the population studied. In table 1, we show the values found. The main differences found in the variables of oxidative stress were determined by the status of NAFLD. **Conclusions.** We found high proportion of NAFLD in heavy smokers; we suggest that they might be a chronic state of oxidative stress caused by smoking. These results confirm that smoking should be considered both as a cofactor in the pathogenesis of NAFLD and its progression.

HEPATIC EVALUATION IN CHILDREN WITH OVERWEIGHT AND OBESITY IN AMBULATORY UNIT SERVED IN THE CITY OF SALVADOR-BAHIA

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Purpose. The purpose of this study was to evaluate the presence of clinical, laboratory and ultrasound changes in children with overweight and obesity followed in an outpatient pediatric gastroenterology and hepatology center at a University Hospital. **Material and methods.** This is a cross-sectional study. Children and adolescents with overweight and obesity were followed in a referral outpatient clinic. The patients underwent a questionnaire, clinical, anthropometric, laboratory and ultrasound evaluation for assessment of hepatic and gastrointestinal complications. The results were analyzed with SPSS, version 13.0. **Results.** The study was initiated in January 2011 and is ongoing. So far 82 patients were evaluated. The mean age was 13.2 years, ranging from 4 to 17 years. Of the total patients, 30 (37%) were male and 52 (63%) were female. Hepatomegaly was identified in 9 (11%) patients. Of the 43 who collected laboratory, 9 (20.9%) had elevated aminotransferases. None of them showed changes in alkaline phosphatase, GGT, prothrombin time and serum albumin. Abdominal ultrasonography was performed in 36 patients. Of these, 9 (25%) had hepatic steatosis, of which 4 (11.1%) mild and 5 (13.9%) moderate. **Conclusions.** Preliminary results show a significant prevalence of clinical, laboratory and radiological findings in these patients. Although NAFLD is very common in the pediatric population, data on the evolution of this condition remain scarce. The simple steatosis may be regarded as a benign condition with little evidence of progression to more advanced stages, while patients with steatohepatitis have a worst prognosis. Thus, it is of great importance that children with overweight and obesity are screened for discovering this condition in still reversible stages.

ASSOCIATION BETWEEN HEPATIC STEATOSIS AND INSULIN RESISTANCE IN CHILDREN WITH OVERWEIGHT AND OBESITY FOLLOWED IN AMBULATORY UNIT

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Purpose. This study aimed to investigate the association between hepatic steatosis and insulin resistance defined by HOMA-IR. **Material and methods.** This is a cross-sectional study. Children and adolescents with overweight and obesity were followed in a referral outpatient clinic. The patients underwent a questionnaire, clinical, anthropometric, laboratory and ultrasound evaluation for assessment of hepatic and gastrointestinal complications. Insulin resistance was diagnosed

by HOMA-IR greater than 2.71. The results were analyzed with SPSS, version 13.0. **Results.** The study was initiated in January 2011 and is ongoing. So far 78 patients were evaluated. Of the total patients, 29 (37.2%) were male and 49 (62.8%) were female. Abdominal ultrasonography was performed in 35 patients. Of these, 9 (25.7%) had hepatic steatosis, of which 4 (11.4%) mild and 5 (14.3%) moderate. The HOMA-IR was calculated in 19 children, being elevated in 11 (57.9%) of them. The association between insulin resistance and estatose showed that the seven children who had steatosis with HOMA-IR calculated, five (71.42%) had insulin resistance (p = 0.515). **Conclusions.** Although the observed data, in certain situations, indicate a positive association, the statistical analysis revealed no statistical significance, possibly by a small number of participants. The data suggest a trend for statistical significance with the progress of the study and expansion of the sample. Although non-alcoholic fatty liver disease is being increasingly identified in the pediatric population, data on the evolution of this condition remain scarce. Thus, it is of great importance that children with overweight and obesity are screened early.

PROINFLAMMATORY RESPONSE OF MONOCYTES AND KUPFFER CELLS IN PATIENTS WITH NONALCOHOLIC FATTY LIVER DISEASE (NAFLD)

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Purpose. Non alcoholic fatty liver diseases (NAFLD) include obesity-related disorders characterized by dislipidemia and hyperleptinemia. Reactive oxygen species (ROS) and cytokines production by Kuppfer Cells (KC) and monocytes (Mo) associate with inflammation and liver damage. We aimed to evaluate the effects of linoleic acid (LA) and leptin (Lep) on ROS and tumor necrosis factor (TNF)α production in Mo and KC and to evaluate the potential anti-inflammatory effect of the antioxidant curcumin (CUR). **Material and methods.** Peripheral blood mononuclear cells (PBMC) and liver biopsies were obtained from adults with NAFLD (NAFLD, n = 11) or individuals with liver diseases non NAFLD (non-NAFLD; n = 6). PBMC from 30 healthy controls (Co) were also included. To evaluate ROS production, PMBC or liver cell suspensions obtained by chemical and mechanical methods were incubated with dichlorofluorescein-diacetate [5 μM], stimulated with Lep[10nM] or LA [200 μM] +/-Cur[30 μM], stained with anti-CD14 and -CD11b mAbs and analyzed by Flow Cytometry. A stimulation index (SI) results from the mean fluorescence intensity (MFI) in stimulated/unstimulated cells. Intracellular TNFα was evaluated in Lep-stimulated [$CD14^+$ TNFα]. PBMC and α fold of increase index (FI) was calculated. Kruskal-Wallis, Mann-Whitney with Bonferroni's correction (p_c), Wilcoxon matched pair test (p_p) and Spearman's rank correlation were conveniently used. **Results.** LA induced a higher production of ROS in Mo from NAFLD (p_c = 0.032 *vs.* Co) which diminished in the presence of CUR (p_p = 0.030). LA similarly stimulated the oxidative burst of KC from patients with NAFLD (p_p = 0.015) and non-NAFLD (p_p = 0.04). Interestingly, ROS production induced by LA in both KC and Mo tend to correlate within NAFLD (r = 0.75, p = 0.06). Leptin induced a high production of TNFa by Mo in Co, NAFLD and non-NAFLD (pp = 0.031; 0.015 and 0.043 respectively) with a higher FI in NALFD (pc = 0.029 *vs.* Co). Though the SI in Lep-stimulated Mo did not differ between groups, NAFLD patients show a tendency to a positive correlation between ROS and TNFα production. **Conclusions.** A proinflammatory effect of LA and Lep on hepatic and peripheral myeloid cells is involved in NAFLD. A blockade of the proinflammatory response with curcumin might contribute to NAFLD treatment.

NONALCOHOLIC FATTY LIVER DISEASE AND CHRONIC HEPATITIS C VIRUS: CLINICAL & HISTOLOGICAL FEATURES

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Purpose. To describe clinical and histological peculiarities of NAFLD associated with HCV. **Material and metdhos.** Cross-sectional study evaluated patients with chronic hepatitis C (CHC) between August 2010 and June 2011. Patients with ethanol intake > 140 g/week, other liver disease or being treated for HCV were excluded. They were submitted to clinical and laboratory evaluation, and liver biopsy. **Results.** We evaluated 42 patients with CHC, mean age 51 ± 10 years, of whom 52.4% women. In biopsy, steatosis was observed in 43%. Patients were classified in G1, those with CHC and NAFLD, and G2, those with CHC without NAFLD. In G1 (18), 66.7% were women and mean age 50.9 ± 10.8. The increase in abdominal circumference (AC) was observed in 61.1%, hypertension in 27.8%, diabetes in 22.2%, dyslipidemia in 27.8%. The mean BMI was 27.6 kg/m², obesity was present in 27.8%. Genotype 1 was present in 60% and 3 in 26.7%. Steatohepatitis was observed in 14.3% (4.8% without fibrosis and 9.5% with fibrosis). In G2 (24), 41.7% were female and mean age 47.5 ± 9.5. The increase in AC was observed in 33.3%, hypertension in 41.7%, diabetes in 17.4%, dyslipidemia in 17.4%. The mean BMI was 24.8 kg/m², obesity was found in 13%. Genotype 1 was present in 76.2% and 3 in 19%. **Conclusions.** The greatest clinical relevancies in patients with chronic hepatitis C and NAFLD in the study sample were: increased abdominal circumference, overweight and obesity, dyslipidemia and genotype 1. The study shows the importance of clinical evaluation of patients with CHC and NAFLD, especially the anthropometric indexes and dyslipidemia.

HEMOLYTIC ANEMIA IN PATIENT WITH LIVER DISEASE ALCOHOL: A CASE REPORT

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Background and aims. The alcoholism is responsible for a variety of pathological effects of hematopoise, directly damaging the precursors of red blood cells causing anemia in presence of chronic ethanol ingestion. Hemolytic anemia is a common clinical condition resulting from the action of alcohol on the lipid membrane of erythrocytes. However, once associated with splenomegaly and direct coombs positive, can set mechanism autoimmune hemolytic. We describe a case of late presentation with good clinical. **Material and methods.** Case report of a patient with hemolytic anemia associated with alcoholic liver disease and literature review of cases previously described. **Results.** GSS patient, 33 years old, single, born in Campina Grande - Paraíba – Brazil, admitted in janeiro/2012 to the Internal Medicine ward of the University Hospital Alcides Carneiro of Campina Grande - Paraiba - Brazil, referring jaundice, ascites and drowsiness had started 20 days ago. Reported alcoholism 21 years ago and had been diagnosed with liver cirrhosis since November/2011. The physical examination showed with regular general state, pallor and jaundice important. Abdomen was distended with splenomegaly. Flapping positive, gynecomastia and vascular spiders were signs of chronic liver disease identified. Initial laboratory

tests showed anemia, elevated indirect bilirubin > direct, relationship AST / ALT < 2 and hypoalbuminemia. It was classified as Child-Pugh C, MELD 32 and discriminant function Maddrey 62. After therapeutic approach, there was partial improvement of clinical picture persisting biochemical changes. Investigation additional with ultrasonography showed ascites, chronic liver disease and splenomegaly with varicose dilatation of the splenic hilum. Viral markers were negative and colangioressonância without lesions of the biliary tract. Autoimmune disease was excluded. We opted for the introduction of steroids (40 mg/day) and during evolution was observed improvement of the anemia, however, persisted elevation indirect bilirubin and reticulocytes. Due to the presence of hypersplenism, hemolysis and Coombs positive hemolytic anemia hypotheisis of autoimmune origin was considered as secondary causes were ruled out. The patient was treated with corticosteroids regression presenting clinical and laboratory. **Conclusion.** The hemolytic anemia should be investigated in alcoholic liver disease patients, especially when the mean corpuscular volume is changed and any increasing in dosage of reticulocytes. Once made the diagnosis, treatment response is fast with good prognosis and decreased length of stay.

ALCOHOLIC LIVER DISEASE IN PUBLIC SERVICE HEALTH IN BRAZIL. CASE REPORT

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Background and aims. The alcoholic liver disease represents an important health problem generating high-cost admissions procedures and achievements. In Brazil, frequency of abuse ranged from 13.3% to 25.2% in the last 30 years and 11% of users are dependent. The amount and duration of intake are important risk factors for addiction causing significant social implications with the increase in traffic deaths. We intend to characterize the profile of a number of cases admitted in our service. **Material and methods.** Prospective analysis of a series of sixteen cases of disease chronic decompensated liver admitted to the internal medicine ward of the University Hospital Alcides Carneiro of Campina Grande - Paraiba - Brazil in the period of twelve months from October 2010. All patients were approached with the questionnaire AUDIT. Prognostic scores were evaluated to define the severity of cases. **Results.** In our study, thirteen patients were considered dependents, predominantly male in fourteen cases. The influence of others was crucial to the contact with excessive alcohol intake (> 10 drinks/day) and duration of consumption above 10 years was significant in the series. The weight loss, anemia and jaundice common manifestations were considered. The Maddrey Discriminant Function was above 32 in six cases, twelve had MELD scores above 15 and seven had APRI ≥ 2. **Conclusion.** The alcoholic liver disease has become a public health problem because of the severity of cases, related to medical care later and missing information. Thus, primary measures of prevention through educational activities in schools can promote control of the cases in society.

MARKERS OF OXIDATIVE STRESS IN PATIENTS WITH NONALCOHOLIC FATTY LIVER DISEASE (NAFLD) WHO UNDERWENT BARIATRIC SURGERY

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Purpose. To evaluate in patients who underwent bariatric surgery, oxidative stress markers and relate them with the progression of nonalcoholic fatty liver disease (NAFLD). **Material and methods.** The study included patients from the Center for Obesity and Metabolic Syndrome who underwent bariatric surgery with intraoperative liver biopsy that confirms the diagnosis of NAFLD. In the pre-operative physical examination was performed with analysis of body mass index (BMI) and bioelectrical impedance analysis. Blood sampling was collected for analysis of serum glucose, insulin, glycated hemoglobin (HbA1c), cholesterol, TGO, TGP and C-reactive protein (CRP) measurement. To determine the oxidative stress, plasmatic lipid peroxidation was evaluated through the technique of TBARS (Thiobarbitutic Acid Reactive Substances) and antioxidant enzyme superoxide dismutase (SOD) activity was evaluated in erythrocytes. The histopathological classification of NAFLD was performed by a blinded pathologist and subjects were divided into a group of patients with steatosis and another with steatohepatitis. For statistical analysis we used the "t" Student test for independent samples ($p < 0.05$). **Results.** From the total of 85 obeses, 28.2% presents steatosis and 71.8% presents steatohepatitis. Steatohepatitis group had higher lipid peroxidation (1.52 ± 0.66 *vs.* 1.04 ± 0.7 nM/mL, $p < 0.001$) and lower activity of antioxidant enzyme SOD (50.99 ± 19.02 *vs.* 81.92 ± 39.98 USOD/mg of protein, $p < 0.03$). Patients with steatohepatitis also showed increased levels of transaminases, CRP, glycated hemoglobin and higher prevalence of insulin resistance. **Conclusions.** Patients with steatohepatitis showed an increase in lipid peroxidation and reduced antioxidant activity enzyme SOD suggesting the involvement of oxidative stress in the progression of NAFLD.

TREATMENT WITH METADOXINE AND IMPACT ON EARLY MORTALITY IN PATIENTS WITH SEVERE ALCOHOLIC HEPATITIS

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Introduction and objective. Severe alcoholic hepatitis (SAH) is characterized by a Maddrey's discriminant function greater than 32, implies 50% mortality at 2 months. Treatment with glucocorticoids has reduced mortality to 35% at 6 months. Kupffer cells activation, proinflammatory cytokines and reactive oxygen species (ROS) production and depletion of mitochondrial glutathione are implied factors in liver injury. Metadoxine (MTD), a synthetic compound based on pyridoxine and pyrrolidone-carboxylate (cyclic amide of glutamic acid and gamma glutamyl, responsible for synthesizing and catalyze glutathione), was shown to inhibit hepatic lipid accumulation. In tissues, ion pair molecules can be separated forming N-oxide molecules that works as rotating traps capable of capturing ROS. The aim of this study was to evaluate the impact of the addition of MTD to standard treatment with glucocorticoid in Mexican patients with SAH. **Material and methods.** Randomized clinical trial, open label, held in Mexico's General Hospital (Registry Key DIC/10/107/03/043). We evaluated 217 patients, 78 met inclusion criteria, and 8 met elimination criteria. We randomized 70 patients with SAH criteria, 35 received prednisone (PDN) 40 mg/day and 35 received PDN 40 mg/day plus MTD 500 mg three times daily. The duration of treatment in both groups was 30 days. Were assessed survival at 30 and 90 days, development of complications, adverse events, and response to treatment (Lille model). **Results.** In the group receiving MTD significantly improved the following pa-

rameters: Survival at 30 days (74.3% *vs.* 45.7% $P = 0.02$); survival at 90 days (68.6% *vs.* 20.0% $P = 0.0001$); there was less development or progression of complications such as encephalopathy (28.6% *vs.* 60.0% $P = 0.008$) and hepatorenal syndrome (31.4% *vs.* 54.3% $P = 0.05$).Response to treatment (Lille model) was higher (0.38 *vs.* 0.63 $P = 0.001$; IC al 95% 0.11 a 0.40). There were not differences between groups regarding the development or progression of variceal hemorrhage, or infection. Adverse events in both treatment groups were similar, mainly epigastric burning, nausea and vomiting. **Conclusions.** The addition of MTD to glucocorticoid treatment improves short-term survival of Mexican patients with SAH and diminishes the development or progression of encephalopathy and hepatorenal syndrome.

ETHANOL REDUCES EGFR EXPRESSION AND PY845 TYROSINE PHOSPHORYLATION IN A HEPATIC CELL LINE

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Purpose. To investigate whether acute or chronic ethanol treatment modifies the total EGFR expression and pY845 EGFR phosphorylation and if those changes are associated with changes in the cell cycle in WRL-68 cells. **Material and methods.** We used the WRL-68 cells, a human hepatic fetal cell lin. Because of ethanol's volatility, a method utilizing sealed containers was used to maintain ethanol levels in the culture medium. Cell proliferation was evaluated using the MTT assay. Cell cycle was analyzed by PI staining and flow cytometry. Total EGFR expression and the pY1086 phosphorylation were carried out by IP and Western blot. All of the data were analyzed by SPSS 17 Real Stat software. The statistical differences were determined by ANOVA followed by a Dennett's multiple comparison. **Results.** We found that ethanol at 50 mg/dL did not modify any of the parameters evaluated. On other hand, ethanol reduced the number of viable cells with concentrations 400 and 800 mg/dL at 72 h. We also found that the treatment of WRL-68 cells with 800 mg/dL ethanol decreased the total EGFR expression and pY845 EGFR phosphorylation. In addition, when cells were exposed ethanol at 800 mg/dL for a short period of time (9 to 15 h), ethanol increased in the percentage of cells in the S phase of cell cycle. **Conclusion.** Ethanol treatment modified the total EGFR expression and pY845 EGFR phosphorylation, and those changes were associated with arrest in phase S of cell cycle in WRL-68 cells.

PEDIATRIC HEPATOLOGY

CONGENITAL HEPATIC FIBROSIS IN THE NATIONAL GUILLERMO ALMENARA IRIGOYEN HOSPITAL Es-SALUD, 2000-2011, LIMA-PERU

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Purpose. The congenital hepatic fibrosis (CHF) is an autosomal recessive disease. It is characterizes by portal fibrosis. The prevalence is 1 in 6,000. CHF is a development disorder that belongs to the family of hepatic duct plate malformation. The aim of our study is to know the incidence, histological and clinical patterns of the CHF in our Hospital between January 2000 and December 2011. **Material and methods.** Retrospective review of the medical charts of the 16 patients with diagnosis of CHF, we described the clinic and demographic characteristics of the patients at the time of diagnosis. Either liver biopsy or a piece of the liver specimen was fixed in formaldehyde 10%, processed and stained with Hematoxilin eosin, PAS, MASSON and Perls. **Results.** 62.5% of the patients were female; 50% of the patients were between 0-5 years of age; the oldest patient was 45 years old, the 37.5% had the previous diagnostic of biliary atresia; and 2% of the last one had histological diagnosis. **Conclusions.** CHF may be present in children or adults, the Colestasis pattern is the aim clinical manifestation, Histological findings: fibrous bands completely surround the irregularly shaped islands of hepatic tissue on jigsaw pattern, Hamartomatous ducts, No liver cells regeneration.

BODY MASS INDEX IN INFANTS WITH BILIARY ATRESIA

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Introduction. An adequate nutritional status of infants with biliary atresia (BA) is important to decrease morbidity and mortality. **Objective.** To determine the nutritional status of infants with BA by body mass index for age (BMI/A) and identify possible associations. **Material and methods.** Prevalence study in 37 infants with BA from Hospital Infantil de México Federico Gómez (HIM), who were seen in demographic variables (age, sex), clinical (portal hypertension: PHT), paraclinical (electrolytes, blood gases, hemoglobin , albumin, glucose, liver and renal function tests), infections (cholangitis, pneumonia, sepsis), hypovolemic (gastrointestinal bleeding, use of blood products), surgery (Kasai surgery, postoperative), personal (vaccination), the histology (cirrhosis) and hospital stay. Statistical analysis included estimation of the prevalence of malnutrition, the estimation of other descriptive measures of interest and association analysis by multiple logistic regressions. **Results.** In this population of infants with BA, with an average age of 4.8 ± 2.5 months found a prevalence of 78,4% of malnutrition, 56.8% of infectious, 62.2% of clinical, 89.1% of hypovolemic and 100% paraclinical complications, respectively. Malnutrition was associated with clinical, histopathological and hypovolemic complications ($p < 0.05$). Infection and vaccination were associated factors ($p < 0.05$). **Conclusion.** Three-quarters of infants with BA had malnutrition, with complications between 56.8-100% and associated with infection and vaccination.

CHARACTERIZATION IN INFANTS WITH BILIARY ATRESIA 1993-1995

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Introduction. Biliary atresia (BA) occurs in 80-90% of infants with neonatal cholestasis. **Objective.** To describe the sociodemographic, clinical, paraclinical, development and management of infants with BA. **Material and methods.** Descriptive observational not experimental study in 22 infants with histopathologic diagnosis of BA from Hospital Infantil de México Federico Gómez (HIM), in which demographic variables were considered, nutritional, clinical, paraclinical, infectious, hypovolemic, surgical, personal, and hospital stay. Descriptive statistics included percentages, means and standard deviations. **Results.** We included 22 infants with 5.6 ± 2.6 months, 59% girls. A predominance of malnutrition and cirrhosis in 82%, respectively, in 73% delay in height, portal hypertension in 55%, 82% use of blood products (68% plasma, packed red blood cells 59%, 23% total fresh blood and albumin, respectively, 14% cryoprecipitate) in 77% antibiotics, 77% history of vaccination, 50% not excreted the dye into the in-

testine and 27% had surgery Kasai. As is often presented: 100% defects in the lab tests (100% liver and 78% renal function tests, 64% of coagulation, 59% electrolyte tests and 42% acid-base tests. Was presented 100% direct hyperbilirubinemia, 82% hypoalbuminemia, 68% anemia, 47% hypoglycemia, 41% hyperaminotransferasemia and 17% thrombocytopenia. The frequency of complications were 95.5% nutrition, 82% hypovolemic (9% bleeding, 36% infectious: 18% pneumonia, 14% sepsis, and 9% cholangitis) and 14% postoperative. **Conclusion.** In these infants with BA, prevailed in more than half of children, female gender, malnutrition, cirrhosis, delayed height, portal hypertension, the use of blood products and antibiotics, history of vaccination, the alteration in the lab tests as direct hyperbilirubinemia, hypoalbuminemia, and anemia and nutritional and hypovolemic complications.

INFANT MORTALITY IN CIRRHOTIC PATIENTS WITH BILIARY ATRESIA 1993-1995

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Introduction. The final stage of biliary atresia (BA) before cancer is cirrhosis, which morbidity is given by the degree of liver dysfunction. **Objective.** To determine the infant mortality in cirrhotic patients with BA and identify possible associations. **Material and methods.** Prevalence study in 27 cirrhotic infants with BA from Hospital Infantil de México Federico Gómez (HIM), who were seen in demographic variables (age, sex), nutrition (undernutrition, delayed height), clinical (portal hypertension PH), paraclinical (electrolytes, blood gases, hemoglobin, albumin, glucose, liver and renal function tests), infections (cholangitis, pneumonia, sepsis), hypovolemic (gastrointestinal bleeding, use of blood products), surgery (Kasai surgery, postoperative), personal (vaccination) and hospital stay. Statistical analysis included estimation of the prevalence of morbidity and mortality, the estimation of other descriptive measures of interest and association analysis by multiple logistic regressions. **Results.** In this population of cirrhotic patients with BA infants, with an average age of 5.2 ± 2.5 months found a mortality of 33.3% and 51.9% infectious, 59.3% clinics, 85.2% hypovolemic, 88.9% nutritional and 100% paraclinical complications. In association analysis found greater chance of dying who had had recurrent infections and Kasai ($p < 0.05$), less opportunity in the vaccinated ($p < 0.05$), finally being associated factors of age, vaccination, PH and malnutrition ($p < 0.05$). **Conclusion.** One third of cirrhotic patients with BA infants died with complications between 51.9-100%; and the mortality was found associated to age, vaccination, PH and malnutrition.

LIVER ABSCESS IN COLOMBIAN CHILDREN

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Introduction. Liver abscess (LA) in developing countries is presented at an early age, being more frequent amebic LA. **Objective.** To describe 14 children with LA from Hospital Universitario del Valle Evaristo García from Cali, Colombia. **Material and methods.** We included 14 children under 15 years of age with a diagnosis of LA for the first time with clinical (fever, hepatomegaly and right upper quadrant pain) and ultrasound findings, in which we analyzed sociodemographic, clinical, paraclinical and evolution. **Results.** Mean age was 9 years, 50% males, with average duration of hospital stay 11 days and 22 days. Also presented vomiting (57%), anorexia and diarrhea (21%), respectively, cough (14%), headache and asthenia (10%), respectively, and malnutrition (43%). The location of the ultrasound was right in 93%, and single in 85%. Other paraclinical showed: albumin (83%), ESR and CRP altered (100%), respectively, and abnormal liver function tests (47%). In 64% in cultures of drainage material identified *E. coli*, *S. viridans*, *S. epidermidis* and *P. aeruginosa*, and 33% amoebae in stools. The duration of medical management was on average 18 days, with various antibiotics and metronidazole in 93%. 71% required ultrasound guided drainage. **Conclusion.** The LA should be suspected clinically with the triad of fever, hepatomegaly and abdominal pain right upper quadrant dominance, and verify the location and type of presentation with an abdominal ultrasound, supported with some paraclinical blood and feces, and initiate a prompt and appropriate medical management with antibiotics, antiparasitic and following a proper evolution to avoid the complications that can lead to increased morbidity and mortality.

RECURRENT HEPATITIS A IN COLOMBIAN CHILDREN

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Introduction. Recurrent hepatitis A is considered one of the different forms of atypical clinical presentation of the hepatitis A virus (HAV). **Objective.** To describe 9 cases of children in Cali, Colombia with recurrent hepatitis A. **Material and methods.** We included nine children between 7 and 13 years (mean age 8.6 years), 56% male with a history of 3 to 5 days, consisting of fever, vomiting, jaundice, abdominal pain and dark urine, IgM positive for HAV, and after 30 days of being asymptomatic, presented again, similar symptoms and IgM positive for HAV. **Results.** The mean liver function tests of the second episode showed: ALT 1,258 U/L, AST 986 U/L, direct bilirubin 5.87 mg/dL and alkaline phosphatase 580 U/L. In all, abdominal ultrasound and serology for autoimmune hepatitis, was normal. None of the children had morbidity associated with recurrent hepatitis A. **Conclusion.** The presentation of recurrent hepatitis A is rare, being reported more than one peak of aminotransferase increases between 3% and 20%, with a satisfactory outcome.

RISK FACTORS PROMOTING NEONATAL JAUNDICE AT ADOLFO GUEVARA VELASCO NATIONAL HOSPITAL ESSALUD CUSCO, PERU

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Objectives. The development of jaundice and hyperbilirubinemia depends of the risk factors, more or less to be investigated in all newborns, for the presence of this alert the physician to the likelihood that the infant developed severe jaundice. In that sense we do this research with the aim of establishing the neonatal risk factors, maternal and parental to the exacerbation of neonatal jaundice in the Neonatology Service at Adolfo Guevara Velasco Hospital, Essalud (HAGV). **Material and methods.** We performed a case-control study from the months of January to June of 2010. The study was approved by the ethics committee HAGV and the Faculty of Biological Sciences at San Antonio Abad del Cusco National University. A card was used to collect clinical data and informed consent was signed by the parents of the unborn. Blood samples were obtained to determine the values of serum bilirubin and hematocrit. Hyperbilirubinemia was defined values of serum bilirubin > 20 mg/dL in the first

24 h. We included 216 cases (infants with clinical diagnosis of jaundice and bilirubin > 20 mg/dL) and 464 controls (healthy children with bilirubin < 1 mg/dL) in a ratio of 1:2. The data from nine risk factors were obtained from medical records and for the determination of polycythemia was considered the hematocrit > 60%. The information was processed in SPSS version 17.0, was performed bivariate and multivariate analysis using chi-square was considered significant $p < 0.05$, to quantify the significant association we calculated the odds ratio (OR) with a CI of 95 %. **Results.** Neonatal jaundice was 19.3%. All risk factors considered in the study were significant. Neonatal factors: male gender (OR = 2.3, 95% CI, 1.7 to 3.3), cephalohematoma (OR = 5.6, 95% CI, 1.7 to 18.0), suffocation (OR = 39.9, 95% CI, 5.2 to 302.0), polycythemia (OR = 83.6, 95% CI, 42.1 to 166.0) and sepsis (OR = 2.0, 95%, 1,2-3,3). Maternal: Presence of UTI (OR = 16.1, 95% CI, 10.5 to 24.7), Application of oxytocin (OR = 36.8, 95% CI, 17.8 to 76.4), cesarean section (OR = 5.3, 95% CI, 3.6 to 7.9) and preterm (OR = 19.8, 95% CI, 13.1 to 29.8), and as a brother with a family history have jaundice (OR = 1.9, 95% CI, 1.3-2.6). **Conclusion.** It is confirmed that neonatal risk factors, maternal and family history of jaundice contribute to the development of jaundice and hyperbilirubinemia in infants HAGV, therefore, must be assessed routinely to prevent morbidity and mortality associated with this disease.

LAS ANGIOPOIETINAS 1 Y 2 ESTÁN INVOLUCRADAS CON EL ESPESAMIENTO DE LA PARED VASCULAR DE LAS RAMAS ARTERIALES HEPÁTICAS EN ATRESIA BILIAR

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Introducción. La atresia biliar (AB) es una enfermedad caracterizada por obstrucción de ductos biliares extrahepáticos y, a pesar de la desobstrucción quirúrgica por una portoenteroanastomosis, suele llevar a la cirrosis. Su etiología no está esclarecida; los autores de este trabajo investigaron la participación de una anormalidad arterial. Se detectó por análisis digital (AD) en la AB la presencia de espesamiento de túnica media en las ramas arteriales hepáticas (ETM) que parece asociarse con la rarefacción biliar (Santos, *et al*., 2005). También se observó que al tiempo de la portoenteroanastomosis el VEGFA, marcador de hipoxia, se expresa en paredes de ramas arteriales tanto en espacios portales como en porta *hepatis* (Edom, *et al*. 2011). Este estudio analizó la expresión de las angiopoietinas 1 y 2 y del receptor Tie2, involucrados en la maturación de la pared arterial, en hígado de pacientes con AB, correlacionando estos datos con el ETM. **Material y métodos.** La expresión de angiopoietinas y receptor fue mensurada por PCRq-TR en muestras de hígado congeladas obtenidas en la laparotomía exploradora que precede la portoenteroanastomosis en los pacientes con AB (n = 22), y en pacientes con colestasis intrahepática de edad semejante (IHC, n = 9). El gene normalizador fue el S18. El espesamiento de túnica media fue evaluado por AD en diez ramas arteriales/imagen a través de la razón "espesor de túnica media/diámetro lumenal" en diez imágenes/paciente obtenidas desde muestras teñidas con H-E. Las muestras se produjeron de material parafinizado colectado durante la portoenteroanastomosis. Otras variables evaluadas por AD incluyeron extensión de la proliferación biliar y densidad superficial de colágeno, relacionadas a la gravedad histológica de la enfermedad. **Resultados.** No fueron encontradas diferencias en la expresión de las moléculas entre pacientes con AB y CIH. Pero sólo en los pacientes con AB se observó correlación moderada positiva entre las expresiones de las angiopoietinas y el ETM (angiopoietina1 r:0.58, P:0.013; angiopoietina2 r:0.52; P:0.032). La expresión de las angiopoietinas se correlacionó negativamente con la de Tie2 (angiopoietina1 r: 0.73, $P < 0.001$; angiopoietina2 r: 0.54; P: 0.007). No se constató correlación entre las expresiones de moléculas angiogénicas y variables asociadas con gravedad histológica. **Conclusiones.** Las angiopoietinas 1 y 2 están involucradas en el ETM en pacientes con AB de una manera no asociada con la gravedad histológica de la enfermedad, y su expresión se correlaciona negativamente con la de su receptor.